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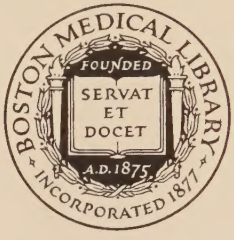

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MENSTRUATION

AND

ITS DISORDERS

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AND

ITS DISORDERS

BY

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GYNECOLOGICAL AND OBSTETRICAL MONOGRAPHS

WITH FORTY ILLUSTRATIONS

D. APPLETON AND COMPANY

NEW YORK LONDON

1924

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THIS BOOK IS DEDICATED

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PREFACE

It is probably not an exaggeration to say that we have learned more concerning the nature and mechanism of the menstrual phenomenon during the past fifteen or twenty years than during many centuries preceding. This new knowledge has been an important factor in the more intelligent treatment of the disorders of menstruation, which constitute a not inconsiderable proportion of the ailments encountered by every general practitioner. The gynecologist and the obstetrician likewise have been given a new light on many hitherto poorly understood problems, by such modern contributions as, for example, that pertaining to the menstrual histology of the endometrium, or that dealing with the endocrine relationships of the ovary.

It would seem, therefore, that the time is opportune for the presentation of a volume devoted to all aspects of the subject of menstruation, both normal and abnormal. So far as I know, there is no other work in any language with exactly this scope. This statement, I believe, will apply even to the rather comprehensive articles in some of the German handbooks. While the present volume is monographic in character, every effort has been made to make it of genuinely practical value, to general practitioners as well as to specialists in gynecology and obstetrics. The surgical treatment of the various forms of pelvic disease which may be associated with disturbances of menstruation has not been considered, for this would mean the inclusion, to all intents and purposes, of a treatise on operative gynecology. For the sake of completeness, however, it has seemed best to include a discussion of certain matters of merely historic interest.

It is hoped that the list of references at the end of each chapter will constitute a good working bibliography for those desirous of going to original sources. These lists are not by any means exhaustive, but the references have been selected as the most worthwhile of the many hundreds which have been consulted in the preparation of this work.

To Drs. Howard A. Kelly and Curtis F. Burnam I am greatly indebted for the chapter on "X-Ray and Radium Treatment of Menstrual Disorders." To Dr. Thomas S. Cullen, professor of gynecology, and Dr. J. Whitridge Williams, professor of obstetrics at Johns Hopkins Medical School, my thanks are due for their helpful criticisms. Finally, it is a pleasure to acknowledge the courtesy and coöperation of the publishers, D. Appleton and Company.

EMIL NOVAK

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MENSTRUATION AND ITS DISORDERS

CHAPTER I

THE SUPERSTITION AND FOLKLORE OF MENSTRUATION

From the very earliest times the phenomenon of menstruation has been the subject of much speculation and study. The older ideas as to the nature of the menstrual process represent a curious blending of speculation and superstition, with very little foundation of real fact. The element of mystery in the phenomenon seems to have inhibited intelligent efforts to study it. Apparently there was a general acceptance of the depressing dictum later enunciated by Colombat, that "the mystery of menstruation will be forever covered with a veil which cannot be perfectly removed." It is gratifying to note that the scientific methods of our own generation have already yielded splendid additions to our knowledge of this problem. Much has been done to dispel the numberless superstitions which formerly befogged the subject in the minds of both the laity and the profession.

Many of these old beliefs concerning menstruation are of interest, and I have thought it might be well worth while gathering some of them together in a chapter which would fittingly introduce the consideration of menstruation from a modern viewpoint.

Even before the time of Hippocrates, menstruation seems to have been looked upon as a cleansing process — a periodic purging of the blood from filth and impurity. The very name given by the Greeks to the process of menstruation (*κάθαρσις*, catharsis) is indicative of this belief in the cleansing function of the menstrual flow. It is still the popular conception among the laity, and perhaps among a certain proportion of the profession. The disagreeable odor of menstrual blood may be in part responsible for this belief.

Pliny spoke of the menstrual blood as being "a fatal poison, corrupting and decomposing urine, depriving seeds of their fecundity, destroying insects, blasting garden flowers and grasses, causing fruits to fall from branches, dulling razors, etc." (Lib. VII, Cap. 15.) Pliny also states that the dog which licks menstrual blood becomes mad, although, curiously enough, as we shall see, menstrual blood was later recommended as a cure

for the bite of a mad dog. He says, further, that "If a woman strips herself while she is menstruating and walks round a field of wheat, the caterpillars, worms, beetles, and other vermin will fall from the ears of corn. Metrodorus, of Scepsos, tells us that the discovery was first made in Cappadocia, and that, in consequence of such multitudes of cantharides being found to breed there, it is the practice for women to walk through the middle of the fields with their garments tucked above their thighs. In other places, again, it is the usage for women to go barefoot, with their hair dishevelled and the girdle loose; due precautions must be taken, however, that this is not done at sunrise, for, if so, the crop would wither and dry up". Astruc is another author who speaks of the ancient belief that the menstrual discharges were so venomous that "they withered and dried up the flowers, marred liquors, tarnished looking glasses, with several other astonishing effects."

Bees, according to Pliny, are said to have an especial aversion to a thief and to a menstruating woman, a glance of such a woman's eyes being sufficient to kill a swarm of bees. Horses are also susceptible to this malign influence. "A mare big with foal, if touched by a woman in this state, will be sure to miscarry; nay, even more than this, at the very sight of a woman, though seen even at a distance, should she happen to be menstruating for the first time after the loss of her virginity, or for the first time while in a state of virginity. So pernicious are the properties of the menstrual discharge that women themselves, the source from which it is derived, are far from being proof against its effects. A pregnant woman, for instance, if touched with it, or if indeed she so much as steps over it, will be liable to miscarry" (Pliny).

Such beliefs are responsible for the abhorrence in which the menstruating woman was universally held. This is perhaps best epitomized in the Mosaic law: "If a man shall lie with a woman having her sickness, and shall uncover her nakedness, he hath discovered her fountain, and she hath uncovered the fountain of her blood, and both of them shall be cut off from among their people" (Lev. XX, 18). The menstruating woman was held to be unclean for seven days, at the end of which time she sacrificed turtle-doves as a burnt offering.

Coitus at such a period was looked upon as a very grave offense. In ancient Persia, the persons guilty of such an act were devoted to the fires of hell until the day of Judgment. The Zend Avesta is full of regulations tending to isolate "unclean" women, while metrorrhagia is condemned as a crime punishable by one hundred strokes of the lash. It is said that even among modern Greeks, menstruating women are denied communion in the church and are forbidden to kiss the church pictures (Ploss). The Bible makes frequent mention of menstruation, though usually in paraphrase. The word "menstruous" is employed three times, and always in the sense of unclean and repellant, as when Jeremiah says "Jerusalem is as a menstruous woman among them."

History tells us, furthermore, that by a decree of the Council of Nice, women were forbidden to enter church while menstruating, so that evidently it was not only the ignorant who entertained the peculiar notions of the uncleanness of women during menstruation. It is even said that certain surgeons would not allow menstruating nurses to assist in operations.

German peasants, according to Ploss, believe that a menstruating woman entering the cellar turns the wine of the Fatherland sour; and that if she crosses a field, she spoils the growth of the vegetation. The humbler class of Jewesses are accustomed to signal their menstrual period to their husbands by a curious ritual observance; they tie bows of blue ribbons to their beds or chairs. Similarly, negresses in certain parts of Africa wear a scarf of glaring color folded three corner wise over the bosom during the menses. Along the Congo River the "house of blood," a hut daubed with red, is used for the purpose of segregating the tribeswomen of each village when in this condition (Knott).

The negresses of Surinam must also, according to Ploss, live apart from their tribes during the menstrual periods. Moreover, when anyone approaches them, they must call out "Mi kay! Mi kay!" — "I am unclean! I am unclean!" The same author also, in his monumental work, "Das Weib," gives innumerable other examples of this almost universal belief among savage and barbarous peoples. A few other examples may be cited of this remarkable taboo put upon the menstruating woman.

In Angola the women are obliged to wear a bandage about the head during the period of menstruation. If bleeding persists beyond this time, the woman is considered to be under the influence of evil spirits, and is punished with one hundred lashes of the whip.

Certain tribes believe that the process is dangerous, not only to others, but to the menstruating woman herself, and so they enforce a strict dietetic regime at that time.

Among the Tinneh Indians, according to Frazer, it is dangerous for a menstruating girl to touch her head with her hand. If she finds it necessary to scratch her head, this must be done with a stick. Among some tribes she is not even allowed to feed herself, and among others, she is obliged to wear hanging from her forehead a fringe made of shells or bones. The purpose of this is to cover her eyes, as she is especially susceptible to the influence of malicious sorcerers at this time (Crawfurd). Among certain races, menstruating women are forbidden to eat anything that bleeds, as this would increase the severity of the flux in the transgressor. Among the Persians, the women are likewise segregated at the time of menstruation. The usual period of isolation is four days; the maximum is nine days.

The Indian women of the Orinoco country in South America are obliged to fast during each menstrual period, while among the North American tribes, the squaws are sequestered in separate huts during menstruation. According to Colombat, the Illinois Indians punished with death any of their squaws who failed to give notice that they were affected by the periodic

discharge. In the same way Crawfurd mentions the case of an Australian black who killed his wife because she had lain on his blanket while she was menstruating. He himself is said to have died of terror within a fortnight.

Among some of the Hottentot tribes the women are made to paint their faces with a spectacle-like design at the time of menstruation. Many savage tribes believe that if a man by any accident comes upon menstrual blood, he will be unlucky in warfare and in all other undertakings.

Ploss quotes a work by Eckarth, published early in the eighteenth century, in which the virulence of the menstrual discharge is illustrated by the fact that, unlike other blood, no amount of washing can remove entirely the stain it produces upon cloths. The same author says that if a menstruating woman looks into a mirror, the latter will forever be marked by two round defects corresponding to the eyes of the woman. This is somewhat similar to the statement of Aristotle that, if a menstruating woman looks into a mirror, not only is the polish lost, but the person who next looks into the mirror will be bewitched. Pliny, speaking of this tarnishing effect on mirrors, says that the polish can be restored by having the same woman look steadily upon the back of the mirror.

Another interesting group of superstitions has to deal with the influence of the menstruous woman upon milk and the milk supply. According to Frazer, the Kaffir woman of South Africa is not allowed to drink milk during menstruation. If she does, the cows from which the milk came will die. The same custom prevails among the Bahimas. Exception is made, however, in the case of the young girl with her first menstruation. An old cow, of small value, is set aside for her use. The underlying belief in these cases is obviously that there is a sympathetic bond of some sort between the cow and the milk, and that any injury to the latter affects the cow also. A menstruating woman is even forbidden to cross the pasture, for if a drop of menstrual blood were to fall on such a place, any cow passing over it would be apt to become diseased and die.

Columella, Graaf, and Verheyen, as well as a number of the old Arabian authors, have likewise attributed noxious qualities to the menstrual blood (Columbat). According to Moreau de la Sarthe, in his "Hist. Nat. de la Femme" (Tome II, 261), the negroes of the South Sea Islands and the aborigines of South America send their females into separate huts and keep them absolutely sequestered during the whole of the menstrual period. Some savage tribes in Africa distinguish by a red flag those huts which contain menstruating women. The color of the flag, evidently, is suggested by the color of the menstrual discharge.

Not all the older writers, it must be mentioned, participated in the view that the menstrual blood was poisonous. Aristotle believed it to be "as pure as that which flowed from any wound." Hippocrates compared it with that of a slaughtered victim ("sanguis autem, sicut a victima, si sana fuerit mulier"). John Freind, in arguing against the prevalent theory of the noxiousness of the menstrual blood, asserts that the latter cannot be

impure, " inasmuch as it is not secreted by the help of any gland, but breaks forth from the capillary arteries, and therefore retains the nature of the arterious, i. e., the most pure blood."

Although such superstitions as we have been discussing are not so common as they were formerly, they are far from being thoroughly rooted out, even in our own day. Ellis speaks, for example, of the regulations still in force in the sugar refineries of northern France, whereby women are forbidden entrance during the boiling or cooling of the sugar, since the proximity of a menstruating woman would cause the sugar to blacken. Dr. Howard A. Kelly tells me that women are not permitted to enter the silver mines in Mexico, as a menstruating woman would cause all the silver to disappear from the veins of metal. For similar reasons no woman is employed in the opium industry at Saigon, it being said that the opium would turn bitter if a menstruating woman were near.

To show that even the medical profession of modern times is not quite free from the influence of such superstition, Ellis quotes several letters written to the British Medical Journal as late as 1878. The writer of one, a member of the British Medical Association, asked whether it was true that if a woman cured hams while menstruating, the hams would be spoiled. She had known this to happen twice. Another medical man wrote that if this were so, what would happen to the patients of menstruating women physicians? Still a third wrote (*British Medical Journal,* April 27, 1878): " I thought the fact was so generally known to every housewife and cook that meat would spoil if salted at the menstrual period, that I am surprised to see so many letters on the subject in the Journal. If I am not mistaken, the question was mooted many years ago in the periodicals. It is undoubtedly the fact that meat will be tainted if cured by women at the catamenial period, whatever the rationale may be. I can speak positively as to the fact."

Knott also speaks of the prevalence of a singular superstition in certain rural communities in England (Wessex and Worcestershire), where menstruating women are believed to have the power of " measling " meats. Laurent, again, mentions a number of modern instances in which such baneful influences were attributed to the menstruating woman — the case of the orchestral performer on the double bass who noticed that whenever he left a tuned double bass in his lodgings during his wife's period, a string snapped; that of the woman harpist who was obliged to give up her profession because at her periods the strings of her harp, and always the same strings, broke; the cases in which women at this period notice the supposedly spontaneous breakage of glasses, the stopping of clocks, etc.

Many other such superstitions might be mentioned — the belief in the poisonous effect of menstrual blood upon cockroaches; the theory of Ambroise Paré, that coitus with a menstruating woman would bring forth monsters; the souring of milk by the proximity of a menstruating woman, etc.

The old belief in the dangerous qualities of menstruation, together with the disagreeable nature of the process to the woman, is perhaps chiefly responsible for the euphemistic manner in which women, especially of the lower classes, are accustomed to speak of it among themselves. As Havelock Ellis points out, the very word "menses" ("monthlies") is in itself a euphemism. Schweig remarks that in both Latin and Germanic countries, the function was commonly designated by some term equivalent to "flowers," indicating, perhaps, that it was a species of blossoming, with the possibility of bearing fruit. German peasant women, for example, according to Schweig, speak of menstruation as the "rosenkrantz" or rose wreath. The Italian women, he further remarks, give it the more high sounding and dignified designation of "marchese magnifico," while the Germans of higher class sometimes use the expression "I have had a letter" to denote the advent of the period.

Similar expressions, as is well known, are made use of among many women in our own country — such expressions as "coming around," "having company," etc. It is interesting to note that such euphemisms are employed even among savage peoples. Ellis quotes Hill Font as recording the use among the Indians of such expressions as "putting on the moccasin," "putting the knees together," and "going outside," the last evidently referring to the custom of secluding the woman in a solitary hut at this period.

There is one other of these ancient superstitions which must be commented upon, and that is the association which has always been made in folklore between woman and the serpent. Whether it was the Satanic rôle of the serpent in the episode of the Garden of Eden which was responsible for this association with the descendants of Eve, it is difficult to say, though this seems a logical assumption. In Germany, it was believed up to the eighteenth century that if one planted in the soil a hair from the head of a menstruating woman, it would be converted into a snake. Among certain tribes in South Australia menstruation is thought to be due to the scratching of the vagina by a bandicoot, which thus causes the blood to flow (Ellis). In Portugal it is believed that women during menstruation are especially apt to be bitten by lizards, and they guard against this risk by wearing drawers during the period (Ploss). It has been pointed out that in various widely separated parts of the world, the snake is believed to be the original cause of menstruation, although no adequate explanation is offered for this deep rooted superstition.

From the belief that menstrual blood is very poisonous, it was, as Ploss remarks, only a short step to the supposition that it might exert a powerful influence against sickness. In an age when physical disease was commonly looked upon as the result of the activity of evil spirits, it is not surprising that the most trustworthy remedies for driving out these enemies of man were usually the most disgusting. Menstrual blood, according to Pliny, was recommended for the following diseases, among others: gout, goitre,

hemorrhages, inflammations of the salivary glands, erysipelas, furuncles, puerperal fever, hydrophobia, epilepsy, worms, headache, etc. As a remedy, Velsh gave menstrual blood the name of "Zenith." It was prepared by extracting the dried blood from cloths by means of Rhein wine or vinegar.

The first napkin worn by a healthy virgin was put aside "for use in cases of plague, malignant carbuncles, and other diseases; it was damped with water and laid on the part; the discharge was also used as a topical application in acute gout" (Crawfurd). Avicenna recommended menstrual blood as an external application for sores of all kinds. For the cure of quartan fever, Ictidas, according to Crawfurd, recommended coitus with a woman who was just beginning to menstruate. The same author states "that medicine men, when about to compound their medicines, were in the habit of making a saving clause that the remedy would be effective, provided no menstruating woman approached their chamber during the compounding process."

Not only as a medicament, but also as a charm, was menstrual blood considered potent. A garment stained with the menstrual blood of a virgin is considered, in parts of Bavaria, a certain safeguard against cuts and stabs. It will also extinguish fire, and is valuable as a love philter (Ellis). Strack gives instances, occurring even in the Germany of today, of girls who administered drops of menstrual blood in coffee to their sweethearts, in order to retain their affections. It is even said (Ellis) that a sect of Valentinians attributed sacramental virtues to menstrual blood, and partook of it as the blood of Christ.

Pliny speaks of the general belief among the Greeks and Romans that a menstruating woman could quiet a tempest, and that she could therefore rescue a ship beset by storm and wave. Daniel Becker (quoted by Ploss) states that if a cloth stained with menstrual blood be fixed on a pole in a field, the hares will congregate to this place in such numbers that they can easily be shot, and even caught in the hand. In certain countries, especially Italy, cloths stained with menstrual blood are said by Eckarth to have formerly been sold as charms against evil spirits. All these superstitions applied, especially, to the menstrual blood passed at the first period.

One more instance of the superstitious belief in the magical potency of menstrual blood may be cited from the prolific Pliny. He states that "if a man takes a frog and transfixes it with a reed entering its body at the sexual parts and coming out of the mouth, and then dips the reed in the menstrual discharge of his wife, she will be sure to conceive an aversion for all paramours."

A monthly purgation of impurities, through the medium of menstruation, was looked upon by many of the old writers as necessary for the promotion of conception. As Freind pointed out, however, if this were true, "no woman would conceive except those who had undergone it, which is wholly repugnant to experience." Other authors (Astruc) suggest that conception is promoted either by "forcibly exciting the woman to coition" or by

the fact that the menstrual discharge opens up the uterine canal, so that the spermatozoön has freer entrance into the uterus."

Mention must also be made of the theory of Galen and his followers, that "the menses are given to women, that they may be evacuated for their health's sake and yield nourishment to the embryo when suppressed by conception." This is the view supported later by John Freind. Hippocrates himself believed that "if a woman with child have her menses, it is impossible that the fetus shall be well, because the growth of the fetus is abated by the menses." In the same belief Celsus stated that "if milk flow from the breasts of a woman with child, whatever she bears must be weakly."

Leaving aside these differences of opinion with regard to the "raison d'être" of menstruation and turning to the direct or "efficient" causes of the phenomenon, it is of interest to note that at least one of the theories prominently discussed among the medical profession, even up to the first quarter of the nineteenth century, was virtually of folklore origin. Certainly it was supported by no scientific observations. I refer to the theory that the rhythm of menstruation is under the influence of the moon.

The fact that the length of the menstrual cycle corresponds to one lunar month led many of the older writers to attribute to the moon a powerful causative influence on the process. "Luna vetus vetulas, juvenas nova luna repurgat". The absurdity of this theory, in accordance with which all women in the same locality would menstruate at the same time, does not seem to have appealed to them.

The celebrated Dr. Mead wrote a treatise on "the influence of the sun and moon on human beings," wherein, according to the prevailing notions of the time, he labored to show that both luminaries exert much action upon animals. In speaking of their influence on periodic hemorrhages, he says "and this action of the moon pertains even to those quadrupeds that menstruate, for it has been observed that they generally have those evacuations about the new moon, in particular, mares and monkeys, and so constantly that, according to the testimony of Horus Apollo, the Egyptians painted the cynocephalus to represent the moon upon account of a certain symptom, whereby the female of this animal has evacuations of blood from the uterus at the new and full moon; and they kept monkeys in their temples in order to point out the times of the conjunctions of the sun and moon, whereon the moon's influence is apparent in all animals, provided irregularities in their way of living do not prevent it."

Among the old authors who adhered to the theory of lunar influences on the menses may be mentioned Aristotle, Van Helmont, and others. Gall, while not admitting any such influence, believed that the discharge takes place generally at about the same time in all women, and that there are certain weeks in which no women are menstruating. He divides the menstrual epochs into two groups, embracing the first eight days of the first and second fortnights, respectively, i. e., the first and third weeks of the month. If women happen to menstruate during the second and fourth weeks, the

occurrence is, according to Gall, accidental, for after some months they again fall under the obedience of the general law.

The other theories as to the cause of menstruation which held sway during the earlier portion of the last century — the ferment theory and the well known plethora theory of Galen — were scarcely less far fetched than the one just discussed, but, inasmuch as they possessed at least a pseudo-scientific basis, they can scarcely be included in a discussion of the folklore of menstruation. They will be discussed in Chapter VI.

The really scientific study of menstruation dates from the work of Negrier, in 1832, although the twentieth century, young as it is, has yielded perhaps the most valuable contributions which have been made to our knowledge of the cause and mechanism of this, one of the least understood of the phenomena of the human body. Modern methods of scientific investigation are gradually sweeping away the cobwebbery of mystery and superstitition which has accumulated about the subject in its passage down the folk paths of the centuries. On the other hand, can we reasonably doubt that our present fine spun theories of menstruation will excite among medical historians of the future, the same compassion which we now bestow upon the crude beliefs of our scientific forbears?

I

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CHAPTER II

PERIODIC SEXUAL PHENOMENA IN THE LOWER ANIMALS

General Considerations.— Much of what we know regarding the physiology of menstruation has been learned from studies upon the lower animals, and is based upon the assumption that there is a close analogy between the phenomenon of menstruation and that of heat or estrus, as exhibited by the lower animals. As we shall see, there is much evidence, both anatomical and physiological, to support this view. The application of the comparative method of study to this problem is of exceeding interest. As might be expected, the primitive manifestations of the function of estro-menstruation are very feeble. As we ascend in the scale of animal life, however, there is a steady and orderly evolution of the process, corresponding to the gradually increasing perfection of development of the reproductive apparatus. The human species presents the highest type of development of the organs concerned in this periodic phenomenon, as well as of the process itself.

Importance of a Study of the Comparative Physiology of Menstruation.— Such comparative studies give a strong promise that the physiology of menstruation may be brought within the domain of scientific knowledge, and thus cease to be the mystery which it has been for so many ages. The possibilities for good resulting from such investigations are great. Most important of all, a knowledge of the real nature of the menstrual process will give us, at once, a rational basis for the therapeutics of the numerous menstrual aberrations. Imperfect as our knowledge still is, a new and intelligent point of view is gained — and gained only — by a familiarity with the analogous phenomenon in the lower animals. No further justification is necessary for a brief survey of what we know concerning the periodic sexual phenomena exhibited by the lower animals, and the application of these facts to the study of the corresponding phenomena in the human female.

Earliest Manifestations of Periodic Sex Activity.— Sexual phenomena of a periodic nature are found throughout the entire animal kingdom, although the primary manifestations of such functions are, as has already been said, rather feebly marked. In the class of animals below the mammalian group, there is of course nothing corresponding very closely to an actual menstrual flow. However, such a flux would scarcely be looked for in them, since they possess no uterus. In the generative canals of these animals, nevertheless, local manifestations of the reproductive

functions are often exhibited in other ways, as by an increased vascularity and pigmentation about the genital orifices.

Wiltshire and others have called attention to the general relation of pigmentation to the reproductive function. In many instances this is very striking. Darwin, for example, says (Descent of Man, page 229) "many birds acquire bright colors and other decorations in the breeding season alone;" and (page 496) "certain ornamental appendages often become enlarged, turgid and brightly colored during the act of courtship." Even in insects, this sexual pigmentation is often very conspicuous. It is interesting to note that the exquisite beauty of flowers, as well as their perfume, are looked upon as sexual phenomena. The same may be said of the bright colors acquired by many birds during the mating season. In this connection, Darwin (page 265) says "The sedentary annelids become duller colored, according to M. Quatrefages, after the period of reproduction; this, I presume, may be attributed to their less vigorous condition at that time."

Many animals of the higher class of mammalia, as we shall see, show the same tendency toward coloring of the external genitalia in connection with the reproductive change. In other animals, such as reptiles, sexual activity is accompanied by an increase in the cutaneous secretions, especially of an odorous variety. Laycock states "many tortoise smell of musk, which probably proceeds from follicles in connection with the cloaca. Several lizards, among others the iguana, have a row of small follicles with round orifices at the inner side of the thigh, which secrete, especially at the coupling season, an odorous, fatty liquid." Darwin states (Descent of Man, page 52) "during the breeding season the anal scent glands of snakes are in active function, and so it is with the same glands in lizards."

Periodic Sexual Activity in the Lower Mammals.— The lowest type of mammal concerning which anything of a definite nature is known with regard to such sexual phenomena as we are now studying is the marsupial. The investigations of Wiltshire seem to show that these animals exhibit a definite period of "heat," and an estrual discharge has been observed. Incidentally, the development of the sexual apparatus in these animals is somewhat more advanced, there being now a vagina, although it enters into the sinus urogenitalis. Practically all creatures of the mammalian family exhibit these periods of heat or sexual excitement to a greater or less degree. Most of the studies which have been made have been upon domesticated animals, or upon wild animals in captivity. It is important to remember, because it has a bearing on the analogous phenomena in the human female, that the sexual seasons of animals may be greatly influenced by such conditions as the climate, the region in which the animal lives, its supply of food, general comfort, and other conditions which differ in wild as compared to domesticated animals.

"Heat" or Estrus.— The classical work of Heape, from which I shall quote freely in this chapter, has placed the study of the sexual season

in the lower animals upon a firm footing. According to this observer, the reproductive period of all mammals, whether male or female, indicates the whole of that period during which the generative organs are capable of the reproductive function. It must be remembered, however, that gestation is not possible at all times throughout the reproductive period. At certain intervals the generative organs of animals exhibit a special activity, while at other times, again, they are inert and fallow. In other words, at periodic intervals, as the result of the action of some peculiar and as yet unknown stimulus, there is an increase in the activity of the sexual glands, culminating in sexual desire, and resulting in coition and gestation. The time during which the sexual organs of an animal exhibit this special activity Heape speaks of as the *sexual season.* It is commonly spoken of as the period of *heat, desire,* or *estrus.* The term *rut* (German *brunst*) is often applied to this state, but Heape states that this is erroneous, inasmuch as this word should have reference only to the phenomena exhibited by the male. The word is derived from the Latin *rugire,* meaning to roar or to bellow, and as Heape says, it is perhaps literally applicable only to such animals as dogs and boars.

In this discussion we are concerned more especially with the phenomena incident to the sexual season of the female. There are two principal types of sexual season exhibited by the mammalian female, the simple or *anestrous* and a more complicated form known of as the *diestrous.*

The Anestrous Cycle.— *The Proëstrum.*— In the simple form, the sexual season is ushered in by the *proëstrum,* or pro-estrous period. During this stage, certain well marked phenomena make themselves evident in the external generative organs and the surrounding parts. The first change usually noted is swelling and congestion of the vulva, with more or less general excitement and restlessness; in addition to these, there are various other signs characteristic of special animals, such as the congested conjunctiva of the rabbit, the drooping ear of the pig, etc. In monkeys, especially, there is often congestion of the face and nipples, as well as of the buttocks and anal region. These parts are often brilliantly colored, as may be observed by the visitor to zoological gardens.

This primary swelling and congestion of the external genitalia is, in most animals, followed by a *discharge from the generative tract.* The nature of the discharge differs in different animals. In some it is made up only of mucus from the uterine glands and those in the lower portion of the generative tract. Epithelial cells are often found in this discharge, coming either from the uterus or from the vagina. Finally, in addition to the above, blood is in certain animals a more or less conspicuous constituent of the discharge. Blood has been observed in the pro-estral discharge of the mare, ass, cow, sheep, bear, pig, cat, rabbit, kangaroo, bitch, and in many types of monkey. It is probable that careful examination of the discharge would show the presence of blood elements in many other animals, as the recent painstaking investigation, carried out on guinea pigs by Stockard and

Papanicolau, would indicate. In some of these animals the blood is present in very small amounts, scarcely enough to tinge the discharge. In others, however, as in the bitch and in certain monkeys, the flow of blood is quite free. Raciborski (quoted by Ellis) observed in the Jardin des Plantes that "the menstrual hemorrhage in guenons was so abundant that the floor of the cage was covered by it to a considerable extent." Moll also speaks of a pair of orangoutangs in the Berlin Zoological Gardens, the female of which menstruated regularly, like a woman, and also refrained from intercourse at the periods. At other times coitus was quite regular, every two or three days. Not only does the character of the discharge differ in different species of animals, but also in different members of the same species, and in the same animals at different times. This applies to both quantity and quality. The analogy to human beings is quite evident.

The *duration* of the pro-estrum appears to be subject to great variations in different animals and in the same animal at different times. In the rabbit it is known to last from one to four days; in the bitch from seven to twelve days; in the monkey from six to eight days.

In regard to the internal phenomena associated with the pro-estrum, Heape makes a division into four principal stages: the period of rest, the period of growth, the period of degeneration, and the period of recuperation. The *resting stage* is that which immediately precedes the pro-estrum, of which it is therefore really not a part. During this period the mucous membrane of the uterus is opaque, white, and anemic. During the *period of growth,* the stroma of the endometrium takes on active hypertrophy, there is marked increase in vascularity, and the mucosa as a whole becomes thick, soft, and congested. In the *period of degeneration,* there is a breaking down of the vessel walls with an extravasation of blood, which becomes collected in little lacunae; the latter rupture, and the blood breaks through the degenerated epithelium to the surface. The *recuperative stage,* as its name indicates, is characterized by regenerative changes in the epithelium and stroma. During this period the blood is expelled, the uterus again assuming the appearance described in connection with the period of rest. These changes I have described thus fully because of their relation to the corresponding changes in women.

The Period of Estrus.— The pro-estrum is followed by the period of *estrus,* which is the climax of the process. This is the period of sexual desire, and it is only at this time that the female is willing to receive the male. The duration is very variable, continuing from a few hours to several weeks. It is interesting to know that, while the period of desire normally follows pro-estrum, it is sometimes evident without the pro-estrum having taken place. This "abnormal estrus" is most commonly seen in connection with congestive or irritative changes in the generative organs. Whether congestion, in itself, is sufficient to produce estrus, or whether some peculiar stimulus through the blood or nervous system is needed, cannot be definitely stated. As a rule, breeders look upon estrus as merely

an accompanying phenomenon of pro-estrum, rather than as a result of it. After the congestion and stimulation of the generative organs associated with pro-estrum has quieted down, it would seem that the organs regain a renewed stimulus, and it is then that estrus takes place. It is not until after the swelling of the vulva and surrounding tissues has been absent for some time that coitus is permitted by most animals. As a matter of fact, where a considerable discharge of blood is present, coitus does not take place until the discharge has almost, if not entirely, been evacuated.

The Metestrum and Di-estrum.— If impregnation does not occur during estrus, the latter is followed by a period during which the activity of the generative organs subsides for a definite time. This is called the *metestrum,* or the metestrous period. In the simple type of sexual season which we are now considering, the metestrum is in turn followed by a prolonged period of quiescence, which is spoken of as the *anestrum,* or the anestrous period. The duration of this is very variable, in some animals two, in others, perhaps eleven or more months. This period of quiescence is finally disturbed by the onset of a new pro-estrum.

The Di-estrous Cycle.— In the more complicated form of sexual season certain variations from the above order of events are observed. Pro-estrum ushers in the sexual season, and is followed by estrus, as in the simple form. This in turn is followed by the metestrum. After this, however, instead of a long anestrous period, as in the simple type, only a short period of quiescence occurs, lasting perhaps only a few days, seldom more than twelve at the most. This is spoken of as the period of *di-estrum,* or the diestrous period. Following this immediately comes a new pro-estrum, the four periods — pro-estrum, estrum, metestrum, and di-estrum — constituting the so-called *di-estrous cycle.* Unless conception should occur, this cycle is repeated two or more times, and may occupy any time from one month to an entire year. If it occurs only during a month or so, it is limited to one particular season of the year; if, on the other hand, it takes place throughout the entire year, it fills the entire reproductive period of the animal. This is the condition of affairs in the human female when the return of the period is not interrupted by gestation.

The Estrous Cycle in Various Animals.— Animals in which only one estrus occurs during each sexual season, or in other words, those which exhibit the anestrous cycle, are spoken of as *monestrous.* Those, on the other hand, which exhibit a series of di-estrous cycles, are called *polyestrous.* It is generally believed that these two types of sexual season are modifications of one another, as a result of the influence produced by conditions of life. For instance, the red deer, according to Heape, is monestrous in the wild state, while in captivity it is polyestrous. Among monestrous animals may be mentioned the bitch, which has two sexual seasons each year, one in the spring and one in the autumn, although there are many exceptions to this rule; some bitches exhibit only one sexual season each year, while in others they may occur at intervals of from four

to eleven months. The wolf and fox are also monestrous. The cat, in the wild state, is said to have one season per year, although there seems to be some doubt upon this point; when domesticated the cat exhibits three or four sexual seasons each year. Among the polyestrous animals may be mentioned horses, cattle, sheep, pigs, certain types of deer, giraffes, elephants and kangaroos. In its most highly developed form, however, the polyestrous type is observed in monkeys and in the human female.

The duration of the di-estrous cycle differs in different animals. For instance, in the domesticated mare and cow it is three to four weeks; in the sheep and pig, two to four weeks; in monkeys it appears to be about one month in duration; while in the human female, as is well known, the usual duration of the menstrual cycle is four weeks. In the human female and also in certain types of monkeys the di-estrous cycle is continuous, recurring all the year around, although there are many exceptions to this rule. Arctic explorers tell us that Esquimaux women, living very far North, do not always menstruate during the long Arctic winters. Not more than 70 per cent, it is said by Cook, show a persistence of menstruation during the long dark depths of winter. It may be, therefore, that a genuine anestrous period is exhibited by these women.

This is of interest as seeming to indicate that conditions of life may bring about a transformation of one type of sexual season into another, even in the human female. In the same connection, Wiltshire reports that in certain savage tribes the women menstruate at intervals of several months, and only at long intervals in the women of Lapland, Greenland, the Faroe Islands, Tierra del Fuego, and in some parts of Paraguay. Although horses, cattle, deer, and the other animals above mentioned, show a consecutive recurrence of the di-estrous cycle when in captivity or under domestication, it is not believed that this is the condition which is natural to them, but that it is the result of the care and attention which they receive from man. As a matter of fact, the only animals known to exhibit the continuous recurrence of the di-estrous cycle in a state of nature are certain types of monkeys. The fact that it is possible to bring about such a striking increase in the capacity for estrus in animals through changes in the conditions of life makes it easy to understand that the regular occurrence of the di-estrous cycle in monkeys and in the human female is only a step in advance of the more or less regular di-estrous and anestrous cycles in the lower animals. Although the sexual season in the human female is continuous, Heape has accumulated many interesting observations which seem to indicate the vestigial existence, as it were, of a special and limited sexual season. I shall quote only a few of them:—

"Feasts, similar to the erotic feasts which were indulged in by the ancients — Babylonians, Phenicians, Egyptians, Greeks, and Romans (Ploss, 1887) — were still practiced to some extent in the sixteenth century in Russia and in some parts of India at a much more recent date, while such customs as 'gwneyd bragod' and possibly our own 'bean feasts' may not

improbably be the modern representatives of these ancient customs in our own country.

"The Watch-and-dies of West Australia and the Tasmanians have sexual feasts in the middle of spring time.

"The Hos, an Indian hill tribe, have a similar feast, which becomes a saturnalia during which absolute sexual freedom is indulged in, in the month of January; while among the Santals, another hill tribe, and the Panjas of Jeypore, a festival in January is kept up for a month, during which promiscuous intercourse is allowed.

"In New Caledonia November (that is late spring) used to be the time when marriage engagements were made, and among the Rajputs of Mewar the last days of spring are dedicated to the god of love.

"Among the Kaffirs of cis-Natalian Kaffirland more children are born in August and September than in any of the other months, and it seems probable this is due to certain feasts during which there is unrestricted intercourse between the unmarried people of both sexes.

"My friend, Mr. Caldwell, tells me that the Queensland natives with whom he was brought in contact have a distinct sexual season in September (that is spring), and that they cannot be prevailed upon to do any work for some weeks at that time of the year."

Are the Phenomena of Estrus and Menstruation Analogous? — I have gone thus fully into the subject of the periodic sexual phenomena exhibited by the lower animals for the reason that it has the most fundamental bearing upon our ideas concerning menstruation in women. Indeed, it would seem to be absurd to expect to be able to appreciate fully the nature and mechanism of menstruation without some idea of the corresponding phenomena in the lower animals. The question which has perhaps suggested itself before this is, *Is the evidence at hand sufficient to justify us in the assumption that menstruation in women is really the analogue of estrus of the lower animals?* I believe that the facts which I have already presented are sufficient to warrant us in drawing this conclusion. The arguments for and against this idea are so well presented by Heape that I cannot do better than to quote them verbatim:

"Those who uphold the homology do so because —

"I. There is congestion of the generative organs during both 'heat' and menstruation.

"II. There may be a recurrence of 'heat' as there is a recurrence of menstruation.

"III. The discharge during 'heat' may be of a menstrual character.

"IV. From a phylogenetic point of view the homology is to be expected.

"These statements may be disposed of together; so far as they go they are true enough, but they are not in themselves, separately or collectively, conclusive evidence.

"Those who deny the homology do so because —

"1. The discharge during 'heat' in the lower animals is said to be mucus, while in the human female it is mostly blood.

"2. The time of 'heat' is said to be the only time the lower animals will permit of coition, while sexual union during menstruation is a very rare occurrence.

"3. 'Heat' or 'rut' is said to occur in both males and females in the lower animals and to depend upon the seasons, whereas in the human species it is said to be not so.

"4. After 'heat' the female of the lower animals is said to refuse the male, whereas in the human female sexual desire is not confined to the time of menstruation.

"5. Heat is necessary to the production of the species in the lower animals, while in woman, 'desire' is said to be not essential to conception.

"6. In the lower animals the ovaries are said to contain ripe ova only during the time of 'heat,' whereas ripe ova are said to be found in the human ovary at all times without reference to menstruation.

"7. There is said to be no proof of the identity of the two conditions.

"I think these propositions fairly cover the ground over which those who deny the relationship of what they call 'heat' to menstruation have hitherto traveled.

"It will be seen at a glance that the denials originate, in most instances, in misconception of the facts, and that many of the errors are due to the misuse of the terms.

"It will be worth while, however, to answer each of them separately, and the following replies are numbered to correspond with the numbers of the above objections.

"1. The discharge in many animals during the pro-estrum contains blood and sometimes uterine tissue; it is not always solely mucus, and when blood is absent it has been shown that its absence is due to a modification of, and not to any radical difference in, the process.

"2. The term 'heat' is here wrongly used; it is made to include both the pro-estrum and the estrus in the lower animals, and is compared in that extended sense with the term menstruation. Coitus does not occur during the pro-estrum, which corresponds with menstruation, but during estrus, which immediately follows the pro-estrum. I have shown above that there is no lack of evidence that the same may be true for the human female.

"3. Although the time for sexual intercourse among human beings is not universally confined to particular seasons, I have shown that in some cases this is so, and that in all peoples there is a marked disposition to indulge in sexual intercourse at particular times of the year, which are entirely comparable to the so-called 'breeding seasons' of the lower animals. Furthermore, in certain domesticated animals and certain wild animals kept in captivity the males do not 'rut' only at certain times of the year, but are prepared to propagate at all times (dog), or almost at all times (captive cattle or deer), throughout the year.

"4. There is some truth in this objection, but it must not be forgotten that, among the lower animals, while captivity reduces the violence of the sexual passion, it increases its frequency; and that in civilized woman, in all probability, it is this variation of the function still further exaggerated which is responsible for the difference (see also 2).

"5. Here again the objection is largely due to a mistaken use of the term 'heat,' which in this case is used to denote estrus.

"Menstruation, that is pro-estrum, in women is as necessary to the production of the species as pro-estrum in the lower animals can be; the fact that estrus is less pronounced in the former is true, but it is not altogether absent, as has already been referred to in the replies to propositions numbered 2 and 4.

"6. This objection has reference to the question of ovulation, which has not been treated of in this chapter; with regard to it I would merely say, that ovulation in certain of the lower mammals is not necessarily coincident with estrus, while in some of them estrus and ovulation are quite separate functions. Ripe ova are not found at all times in each human female, and that they may be found at times which are not coincident with menstruation, is merely further evidence that these functions are independent also in women. Further, the degree of independence which these two functions assume is apparently variable in the human female.

"7. The answer of this objection is contained in the foregoing."

II

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CHAPTER III

THE SOURCE OF THE MENSTRUAL FLOW

The Endometrium the Source of the Menstrual Blood.— The mucous membrane of the uterus is the immediate source of the menstrual blood. This does not, however, apply to the mucous membrane of the entire uterus, but only to that which lines the corpus uteri or body of the uterus, i. e. that portion above the level of the internal os. To this portion of the mucosa the term " endometrium " is applied.

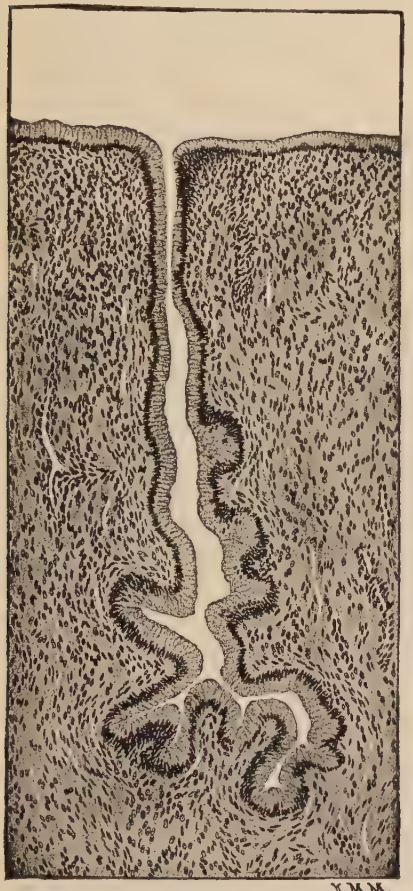

FIG. 1.— NORMAL CERVICAL GLAND (Williams).

The Rôle of the Cervix Uteri.— There is a decided difference between the structure of the endometrium and that of the cervical mucosa or endocervix. (Figs. 1 and 2) Corresponding to this anatomic difference between the two structures, they exhibit also a well marked functional difference, inasmuch as the cervical mucosa, according to most investigators, has no part, under ordinary circumstances, in the production of the menstrual blood. It is true that from time to time cases are observed in which menstruation persists even after supravaginal hysterectomy, and that such cases are explained by some on the theory that the cervix also participates actively in the menstrual process, and is responsible for its continuance even after removal of the entire corpus. It is probable that in most of these cases a strip of endometrium has been left behind, and that it is this which keeps up menstruation. As a matter of fact, the purposeful retention of such a bit of endometrium has been recommended with the idea of preserving the menstrual function in cases in which supravaginal hysterectomy is necessary. At any rate, what-

ever may happen in the exceptional case, there is no good reason to believe that the cervix plays an active part in normal menstruation.

In this connection it is interesting to note that there has been some discussion as to the *size of the cervical canal during menstruation.* Some have claimed that the lumen of the canal is narrowed by the swelling of the mucous membrane; others that it is dilated. Most of these statements appear to be mere expressions of opinion. The only actual measurements, so far as I have been able to ascertain, have been made by Herman, who concluded that there is a slight spontaneous dilatation of the canal during menstruation, reaching its maximum on the third and fourth days. This perhaps explains why the pain in certain cases of dysmenorrhea is apt to be relieved after the first day or two of the flow.

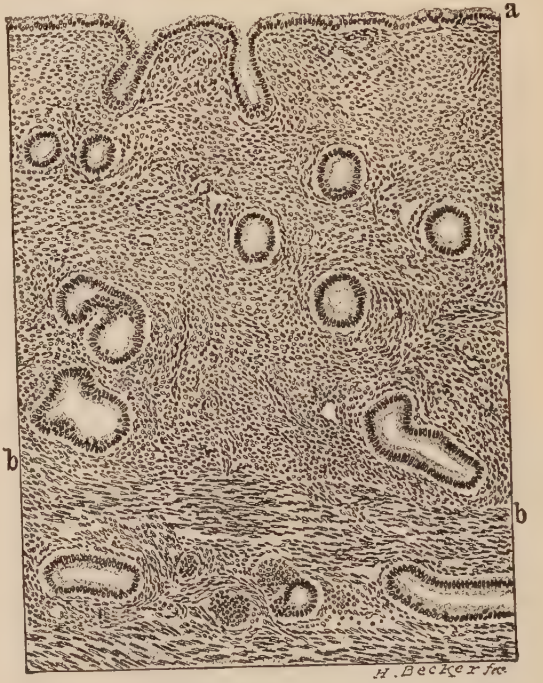

FIG. 2.— NORMAL ENDOMETRIUM (Cullen).

Compare epithelium, glands and stroma with those in Fig. 1.

Do the Fallopian Tubes Participate?— A question which has excited much discussion, and which is even yet unsettled, is the relation of the fallopian tubes to menstruation. Do they, like the body of the uterus, exhibit certain characteristic changes at the time of menstruation, and do they help in the elimination of the menstrual flow? These questions are answered differently by different observers. There are some who believe that the tubes play only a passive role in menstruation. Others again consider the tubal mucosa an active factor in the process, stating that it exhibits histological alterations just as does the endometrium, though to a less degree. Unfortunately, the statements of many authors are not of scientific value, for there is still a " plentiful lack " of reliable observations on the subject. Furthermore, the evidence already in hand is quite conflicting, so there is need of much more work upon the subject.

CLINICAL EVIDENCE.— A large number of cases has been recorded in support of the theory that the tubes do participate in the menstrual process. Bland's case was one in which there was a discharge of blood each month from a sinus resulting from an old operation. It was later found that the fimbriated end of the right tube had become adherent to the scar, so that the lumen opened directly on the exterior. Chapin Minard's case, again,

was one in which blood was seen to emerge from the tubal ostia in a case of inversion of the uterus. Other cases have been reported by Leopold, Sutton, Hennig, Landau and Rheinstein, Courrant and others.

In the majority of these patients, the existence of tubal menstruation was determined by a discharge of blood at the menstrual periods from sinuses communicating with the lumen of the tube; from a stump of the tube when this had healed into an abdominal cicatrix; or from the uterine orifices of the tubes when these were rendered visible by inversion of the uterus. The cases belonging to the first two groups are open to the objection that there is no way to determine whether the blood has really been given off by the tubal wall or whether it has merely entered the tube from the uterine cavity. The difficulty in ascribing the blood to a genuine menstrual function of the tube is increased by the fact that we are not, in such cases, dealing with normal tubes, but with tubes which in most instances are the seat of pronounced pathological alterations, and which might in themselves be the cause of a hemorrhagic discharge, especially during the period of pelvic congestion associated with menstruation.

As regards the cases of inversion of the uterus in which a discharge of blood has been noted from the exposed uterine orifices of the tubes, certainly such profoundly pathological cases as these can not be utilized to prove or disprove the participation of the tube in the process of normal menstruation. The circulatory disturbances which must inevitably be associated with such a condition as long standing inversion of the uterus might well explain the occurrence of a bloody discharge from the tubes at the time of menstruation, without actually stamping it as a genuine menstrual discharge.

Histological Evidence.— As Czyzewicz has pointed out, the only reliable method of determining whether or not the tubes take part in the menstrual process is by means of microscopic examination of normal tubes removed at the time of menstruation. Such specimens may be obtained postmortem from women who have died suddenly during the menstrual period as a result of some disease which in itself would not influence menstruation. Or, perhaps better, they are occasionally obtainable through operation performed at the menstrual period — operations, for instance, in which the sound tubes are removed with the uterus in the course of a supravaginal hysterectomy. To be of value in such a study the removed tubes must be free from pathological change, they must not be injured in removal, and they must be placed at once in the fixing fluid. In addition, there must be an accurate history of the case, especially from the standpoint of the menstrual dates and the freedom of the patient from any condition, whether general or local, which might influence the periodicity of menstruation.

Czyzewicz describes the results of his studies in six cases in which all these requirements seem to have been rigidly observed. His technic appears to have been scrupulously careful, and so far as I have been able to learn, his study is the only one to which no exception seems possible on this score.

One of his cases was operated upon on the first day of menstruation, one on the second, and the others on the fourth, sixth, seventh, and fourteenth days after the onset of a menstrual period. He concludes from this study that typical blood elements are to be found in the lumen of the healthy tube during the menstrual period, and not in the intermenstrual period. This, however, is not equivalent to saying that the blood is tubal menstrual blood, i. e., that it has found its way out from the tubal vessels by rhexis or by diapedesis, for there is a possibility that it has made its way into the tube from the uterus, or even from the abdominal cavity.

Czyzewicz brings forth a number of facts in support of the view that the blood does not spring from the tubal vessels. In the study of a large number of sections he failed to observe any actual extravasation of blood from a ruptured vessel into the surrounding tissue, nor could he establish any direct connection between the red blood corpuscles within the blood vessels and those within the tubal lumen. As additional evidence against the theory of tubal menstruation may be mentioned the fact that the epithelium in tubes removed at the time of menstruation shows no noteworthy changes. There is an absence both of cellular degenerative changes and also of any such heaping up of the epithelium as would be produced by escaping blood.

As a result of his investigations, Czyzewicz concludes that the tubes do not participate in the process of menstruation, although at the menstrual epochs there occurs a dilatation of the tubal blood vessels similar to that seen throughout the generative tract. The blood, however, does not leave the blood vessels. The blood elements that may be found in the tube at the time of menstruation have probably been forced into it by uterine contractions at that time. Just what becomes of this blood is not easy to say. From the fact that phagocytes are not found in the tube in these cases, Czyzewicz believes that in all probability the blood is not absorbed in the tube, but makes its way back into the uterine cavity, being assisted in this movement by the downward propulsion of the cilia.

Most of the cases which have been reported as examples of tubal menstruation have not been studied with sufficient accuracy or thoroughness to make the findings of much value in this regard. A fairly thorough reading of the literature of the subject leads me to believe that there is not at the present time any incontrovertible evidence of active participation of the tubes in the menstrual process. In a number of laparotomies performed during menstruation, in which the tubes were carefully examined from this standpoint, I have never been able to detect the presence of blood in the tubes, although the limitations of gross observations of this sort are obvious.

III

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CHAPTER IV

MENSTRUAL CYCLIC CHANGES IN THE UTERUS

HISTORICAL

The earliest studies on the anatomy of the menstruating uterus were made by Kundrat and Engelmann, whose material consisted of uteri obtained from cadavers. Even with their undeveloped methods these workers described certain changes as characteristic of the premenstrual period — the widening of the glands, the dilatation of the blood vessels, and the round cell infiltration of the interglandular tissue. Another early investigator who utilized the uteri of cadavers for his work was Williams, nine of whose cases had died of acute infectious diseases, thus rendering his results much less valuable. Leopold, on the other hand, selected only uteri removed from women who had died very suddenly, and whose previous menstrual histories showed no abnormality. He found that shortly before the onset of the menstrual bleeding, the mucosa swells, partly as a result of cell growth, and partly as a result of edema. The superficial capillaries are widened, and for several days there is an escape of blood into the surrounding tissue. As a result, the epithelium and the upper cell layers are pushed off. Leopold did not, however, agree with Williams in the view that the destruction of the mucosa is complete. Wyder endeavored to settle this point by a study of the menstrual secretion obtained by means of an aspirating syringe. In this he found desquamated epithelial and stroma cells, although he was later contradicted in this respect by De Sinéty.

It was Möricke who first avoided the use of dead material by studying the scrapings from 45 women in various stages of the menstrual cycle. He concluded that the mucosa remains quite intact throughout the process. Perhaps the most fruitful early work on the subject, however, was that of Westphalen. This investigator studied curettings and freshly extirpated uteri. He found that about ten days before the beginning of menstruation there begins a serous or sanguinoserous edema of the mucosa, which presses apart the meshes of the stroma. Marked blood vessel dilatation does not occur until the beginning of the flow. The glands increase in number, become tortuous, and are often filled with secretion. At the end of menstruation the epithelium constitutes an almost complete covering, showing interruption only in pathologic conditions. The characteristic regeneration begins a few days after menstruation, being marked by the appearance of numerous mitoses which during menstruation are noted only sporadically.

The regeneration involves the mucosa as a whole, the stroma as well as the glands and the epithelium. Its climax is reached about fourteen or fifteen days after the beginning of the bleeding. Westphalen speaks of the time from the eighteenth day to the beginning of the next menstruation as the "period of rest." It may thus be seen that, in large measure, Westphalen anticipated our modern views of the menstrual anatomy of the uterus, as based upon the later work of Hitschmann and Adler.

Even such a brief historical resumé as this would be incomplete without reference to the work of Gebhard. Up to quite recent years, it was his description of the anatomic changes in connection with menstruation which was most generally accepted. This author divides the process of menstruation into three stages: *First,* the stage of *premenstrual congestion.* Before the beginning of the flow there occurs a marked dilatation of the capillaries and a widening of the stromal meshes, which are filled first with a serous fluid, then with blood elements. As the blood, which breaks through the capillaries, increases in amount, it is driven to the point of least resistance, i. e., the surface. The lifting of the epithelium by the blood forms the so-called "subepithelial hematomata." *Second,* the stage of *external hemorrhage.* In this stage, the hematomata open and discharge their blood on the surface, i. e., into the uterine cavity. *Third,* the stage of *postmenstrual regeneration.* The disappearance of the swelling is looked upon as due to the bleeding. The blood in the tissues which has not reached the surface disappears gradually through resorption, or is converted to a yellowish or brownish pigment which withstands absorption for a considerable while. Other valuable investigations of the menstrual histology of the uterus have been made by Mandl, von Kahlden, Löhlein, Van Meerdervoort, Jakobs, Herman and Wendeler.

MACROSCOPIC CHANGES IN UTERUS AT MENSTRUATION

Perhaps the most conspicuous macroscopic change occurring during menstruation is the pelvic hyperemia so characteristic of the process. The pelvic vessels, especially those of the uterus and adnexa, are engorged with blood. Operations performed at this time are usually attended with much more hemorrhage than at other times. The uterus, as a result of this influx of blood, becomes slightly enlarged, bluish red in color, and rather soft in consistency.

THE ENDOMETRIUM

Macroscopic Changes.—Aside from the congestion of the endometrium, with a consequent reddish, engorged appearance, the most conspicuous gross change is in its thickness. According to Döderlein the greatest thickness which is noted physiologically, i. e., in the absence of pathological alteration, is about 7 mm., although Schröder has found it in some cases to reach the thickness of 8 mm.

The portion of the endometrium which becomes thus thickened is the so-called superficial or "functional" layer. The compact layer, or, to use the term employed by Schröder, the basal layer, is of practically constant thickness, usually 0.7 to 1.2 mm. The cause of the increase in the thickness of the endometrium is threefold: (1) the increase in the size of the epithelial cells, owing to the secretory activity; (2) the increased amount of blood in the blood vessels; (3) the greater or less degree of edema always found just before menstruation.

Histological Changes.—Within recent years considerable light has been thrown upon the study of menstruation by an increased knowledge concerning the histological changes which occur in the endometrium during the various phases of the menstrual cycle. In order to appreciate the changes which recent investigations have brought about in our conception of the structure of the normal endometrium and of its changes at various periods, one need only read the descriptions to be found in the older text books of gynecology and anatomy.

Structure of Normal Endometrium.— In the usually accepted sense, as already stated, the endometrium is the corporeal portion of the uterine mucosa, i. e., the portion above the level of the internal os. It is best described as consisting of a surface epithelium, glandular elements, and an interglandular tissue known as the stroma.

The *epithelium* is of the ciliated columnar variety, differing from that found in the cervix in that the cells are not so tall and not so slender; that the nuclei take a paler stain, and are situated near the center of the cells instead of near the basement membrane; and that the protoplasm takes an acid stain, while that in the cervix not uncommonly takes an alkaline stain on account of the excessive amount of mucus which it contains. (See Figs. 1 and 2)

The *glands* are of the simple or branched tubular variety, and are lined by epithelium continuous with and similar to that on the surface. The glands extend down to the muscular coat of the uterus, and not infrequently penetrate the muscle to some extent, carrying with them an enveloping mantle of stroma.

According to most authors the *stroma* is made up of a delicate reticular network of fibrillar connective tissue, containing in its meshes large numbers of oval or spindle cells. At the present time there is no unanimity of opinion as to the exact nature of the stromal tissue. Nagel and Waldeyer believed it to be of a lymphatic type and compared it to the stroma of the intestinal mucosa; Leopold regarded it as a spread out lymphatic gland *(lymphdrüsenfläche),* while Johnstone considered it to be of an adenoid type. Most authorities accept the view of Minot, that the stroma is merely a form of embryonic connective tissue, and this is probably correct.

Modern Views as to Menstrual Histology of the Endometrium.— From a physiologic point of view the endometrium bears an important relation, whether active or passive, to the function of menstruation, and it

would be interesting, if space permitted, to trace the various views which have at different times been held as to the changes in the endometrium at the time of menstruation. Unfortunately, up to recent years the extent of these changes has been gauged largely by the comparative study of menstruating and non-menstruating uteri, and there has been no systematic effort to study the histologic structure of the endometrium from the begin-

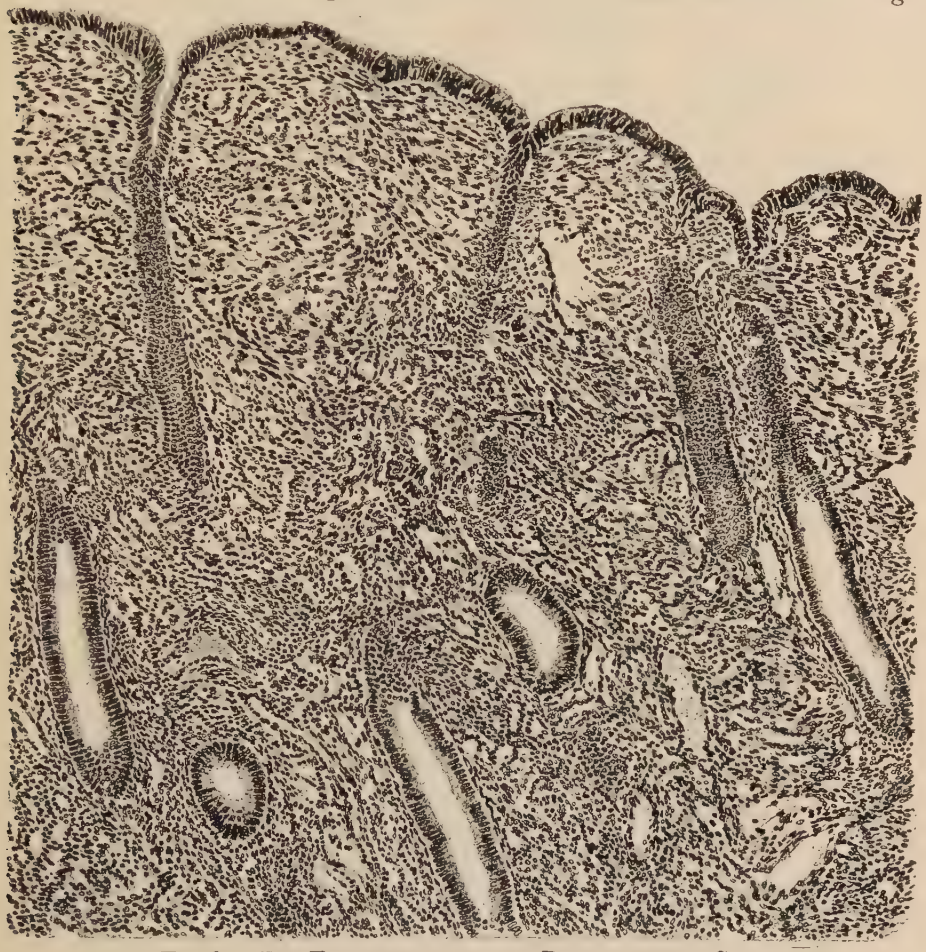

FIG. 3.— THE ENDOMETRIUM IN THE POSTMENSTRUAL STAGE.

Note especially the straight, narrow, collapsed glands.

ning to the end of the menstrual cycle. In 1908, however, an important contribution to our knowledge of this subject was made by Hitschmann and Adler, whose work has revolutionized our former ideas of the histology and pathology of the endometrium. These observers, after a painstaking study of the uterine mucosa from 58 women at various periods of the menstrual cycle, were able to demonstrate quite clearly that the uterine mucosa undergoes a cyclical histological change which corresponds to the clinical

cycle of menstruation. This developmental cycle in the endometrium they divide into four stages, as follows:

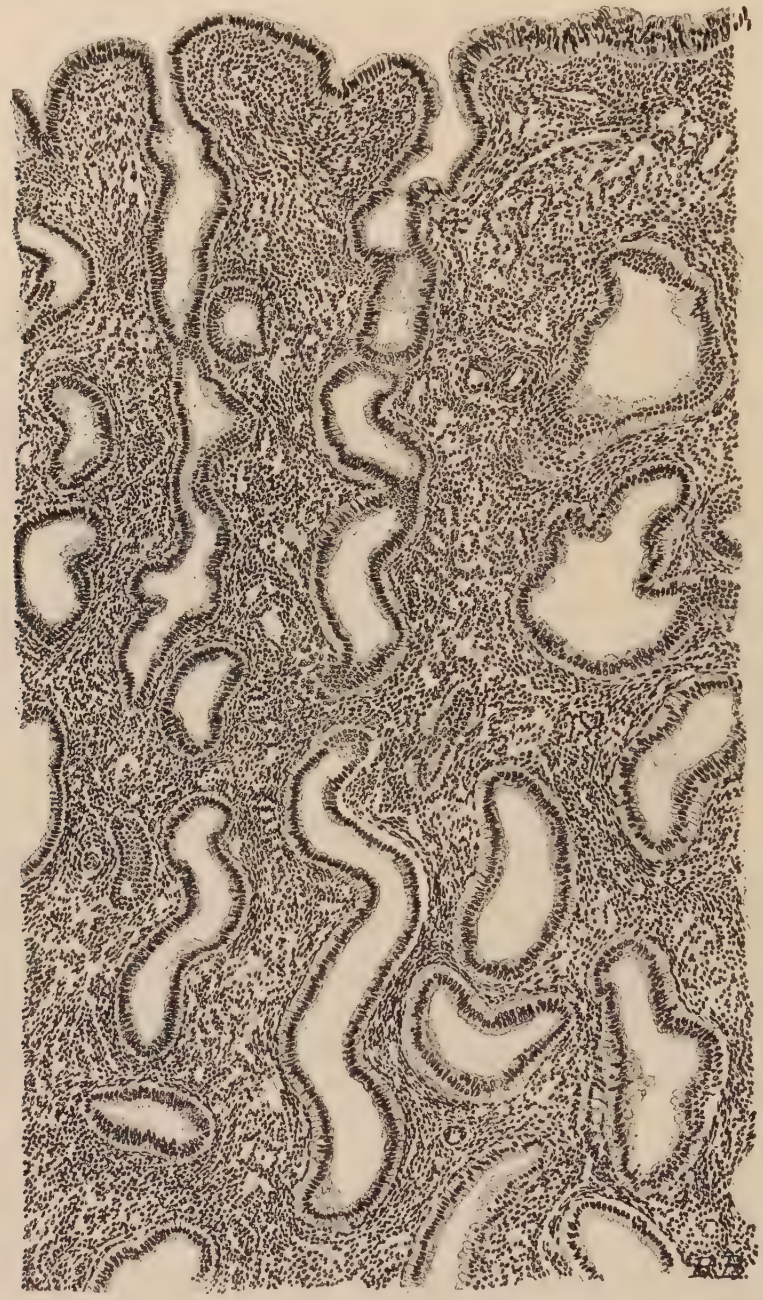

FIG. 4.— THE ENDOMETRIUM IN THE INTERVAL STAGE.

The glands are undergoing a gradual hypertrophy, being now moderately tortuous. The stroma is still rather dense and compact.

FIG. 5.— THE ENDOMETRIUM IN THE PREMENSTRUAL PHASE. The glands are markedly hypertrophied, so that on longitudinal section they are saw-like in appearance, while on cross section they show a characteristic scalloping. The epithelium gives evidence of secretory activity, being low, mucoid and "frayed." The typical decidua-like appearance of the stroma is well shown in the superficial layer of the endometrium.

The Postmenstrual Stage, embracing the few days immediately following menstruation. During the latter it seems as if the endometrium empties itself, as it were, so that during the postmenstrual period its glands are narrow, collapsed, and straight, while the stroma is rather firm and compact (Fig. 3).

The Interval Stage is the term applied to the long period between the termination of the preceding stage and the beginning of the premenstrual phase, next to be described. During this period the endometrium is undergoing a steady but gradual development, the glands becoming fuller and exhibiting gradually increasing convolution. The stroma is still quite compact in appearance (Fig. 4).

The Premenstrual Stage begins from a few days to a week or more before the next menstruation. At this time, according to Hitschmann and Adler, there is a sudden increase in the hypertrophic development of the endometrium. The lumina of the glands become much

increased, presenting a characteristic scalloping on cross section, while in longitudinal section they exhibit a dentate appearance (*sägeförmige drüsen*). In very marked cases there is a strong resemblance to the glands of early pregnancy. The epithelium undergoes a mucoid change, often appearing low and shreddy. The stroma cells participate in the general process of development, and in exaggerated instances may show such a protoplasmic increase as to simulate very closely ordinary decidual cells. More frequently, however, there is only a suggestion of this change, the cells being of a transitional type (*decidua-ähnliche zellen* or *übergangszellen*). (Fig. 5)

The Menstrual Stage, corresponding to the actual existence of menstruation, is characterized microscopically by appearances which are to be looked upon as a transition from those of the premenstrual period to those of the postmenstrual phase. In addition to the vascular phenomena

FIG. 6.— ENDOMETRIUM ON SECOND DAY OF MENSTRUATION.

Some of the glands are still large and hypertrophied; others have become small and collapsed, as in the postmenstrual stage. There is marked injection of the small capillaries and venules, while lacunae of blood are often seen in the tissues. As will be seen from this section, extensive loss of the epithelium is not a characteristic feature of menstruation.

characteristic of this stage, one finds usually that some of the glands are still very hypertrophic, while others already show the collapse characteristic of the postmenstrual stage. A similar transition is noted in the stromal tissue. (Fig. 6)

In the eleven years which have elapsed since the publication of the work of Hitschmann and Adler, many articles have appeared in confirmation of their results, and a few in which a greater or less degree of contradiction is expressed. Among the more important of the latter may be mentioned those of Henkel, and Keller and Schickele. Both of these, however, have been very adequately answered in the recent exhaustive review of the subject by Hitschmann and Adler. At any rate, the weight of evidence at the present day is overwhelmingly in favor of the general correctness of their teaching, although on certain details there is still room for discussion.

It is an interesting commentary on the rapidity with which our knowledge of such subjects is changing to call attention to the fact that already a revision of this description is offered by Schröder, who has done such excellent work along these lines. This author believes that the entire functional layer of the endometrium is lost at each menstrual period, being regenerated from the glands of the basal layer. The period of desquamation and regeneration, according to Schröder, embraces a period extending from the first to the fifth days of the menstrual cycle, counting from the day of menstrual onset. Following this comes the proliferative phase, during which the glands exhibit progressively increasing proliferative changes, although no signs of secretory activity are evident during this period. The proliferative changes in the glands, Schröder explains, are due to the maturing follicle. Ovulation takes place about the fifteenth day of the cycle, and the corpus luteum thús formed is the cause of the secretory activity of the gland epithelium, reaching its climax just before menstruation.

Schröder's division of the menstrual cycle, therefore, is into three stages: (1) the *stage of desquamation and degeneration,* extending from the first to the fifth days of the cycle; (2) the *proliferative stage,* from the fifth to the fifteenth days; and (3) the *secretory stage,* from the fifteenth to the twenty-eighth days. The work of Schröder, if confirmed by subsequent studies, will mark a big step toward the study of the true relation of menstruation and ovulation, as will be discussed in a subsequent chapter.

Changes in Epithelium during Menstrual Cycle.— An important factor in the structure of the endometrium is, of course, the epithelium, and upon its alterations are largely dependent the variations in the appearance of the endometrium at different stages of the menstrual cycle. This is especially true of the differences in the appearance of the glands at different phases of the cycle, and also of the varying thickness of the uterine mucosa.

It has been asserted by Theilhaber and others that the epithelial cells of the corpus uteri, like those of the cervix, functionate continually; but this is denied by Schröder, who emphasizes that secretory activity is character-

istic of the premenstrual and the latter portion of the interval periods — in other words, that it begins only after the formation of the corpus luteum, upon which it is dependent. (See Chapter V.)

In the postmenstrual period the epithelium, some of which is lost during

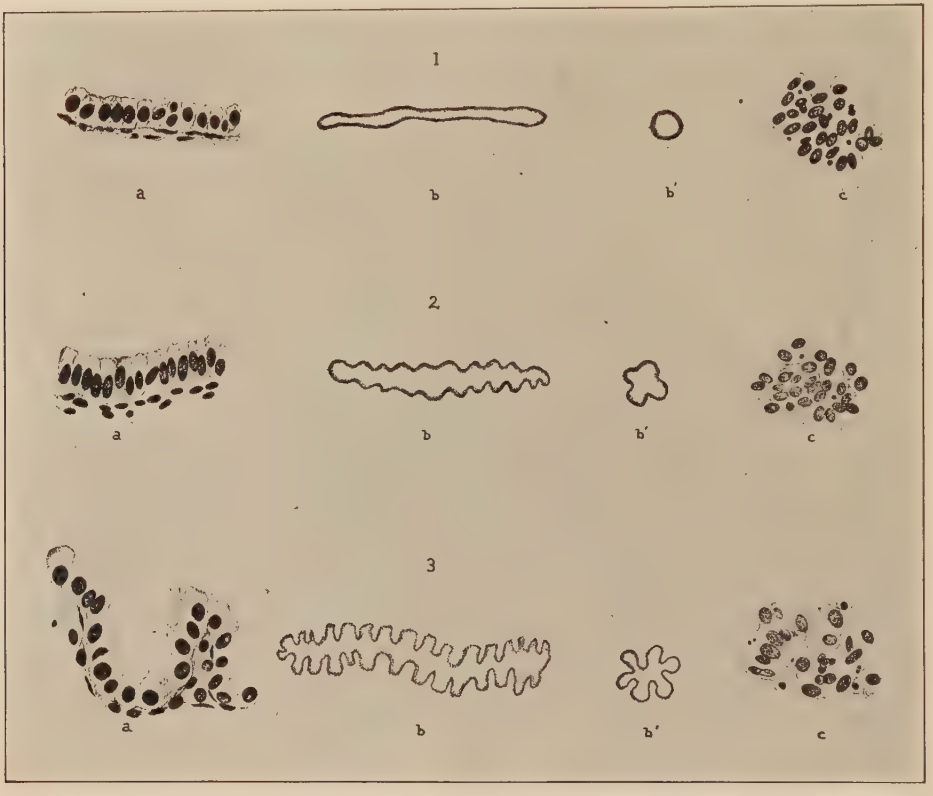

FIG. 7.— THE CHARACTERISTIC CHANGES IN THE UTERINE EPITHELIUM, GLANDS AND STROMA AT THE VARIOUS PHASES OF THE MENSTRUAL CYCLE.

1.— The postmenstrual stage; (a) epithelium, (b) gland in longitudinal section, (b^1) gland in cross section, (c) stroma.

2.— The interval stage; (a) epithelium, (b) gland in longitudinal section, (b^1) gland in cross section, (c) stroma.

3.— The premenstrual stage; (a) epithelium, (b) gland in longitudinal section, (b^1) gland in cross section, (c) stroma.

N. B.— The menstrual stage is not illustrated, as it represents a transition from (3) to (1).

menstruation, is low and cuboidal, slowly becoming higher later in the interval. During the premenstrual period the cells are bloated and in many cases granular or rather shreddy, as a result of their active secretory function (Fig. 7).

Changes in Uterine Glands during Menstrual Cycle.— The glandular changes are much more striking and much more constant than those noted in the stroma, and therefore constitute the more reliable and convenient criterion of the degree of menstrual reaction in the endometrium. In only a comparatively small proportion of the cases is there such a striking overgrowth of the stromal cells that they are at all likely to be mistaken for genuine decidual cells. On the other hand, a greater or less degree of gland hypertrophy, easily appreciable on microscopic examination, is quite constant. It must not be assumed that the glandular phenomena are primary in character. Like other mucous glands, the uterine glands are merely reduplications of the mucous membrane, the evident purpose of which is to increase the secreting surface. When the glands show dilatation of the lumina and exaggerated infoldings, as they do in connection with the premenstrual hypertrophy, it is because the individual cells are swollen and overgrown. Room is made for these enlarging cells by increasing convolution of the glands.

The old rule of Gebhard that the glands are to be considered abnormal if the distance between them is less than four or five times the diameter of the glands, has long since been shown to be incorrect, for there are wide normal variations in different mucosae in this respect. Moreover, in the examination of curettings, the microscopic appearance as to this point varies in different portions of the endometrium and even more at different depths of the mucosa. When one considers the individual variations in different women, with regard to the duration and amount of the menstrual flow, it is not surprising that there should also be a wide variation in the degree of gland changes exhibited at the premenstrual period. As Hartje has pointed out, there is a gradual progression from the straight, collapsed gland of the postmenstrual period to the gland at the height of premenstrual development — the gland with papillary ingrowths and perhaps secondary alveoli. In the more marked cases the glands are very much widened. The stroma is diminished, so that the glands are almost in contact and the epithelium is swollen with secretion. Many of the glands show well marked papillary projections into the lumen, or in the less marked cases take on a saw-like appearance (*sägeförmigedrüsen*). (Fig. 5.) Such glands as these were at one time considered pathognomonic of pregnancy (Opitz), although recent investigations have shown clearly that this is not the case. Schwab, for example, in his examination of a series of 41 curettings, found Opitz's "pregnancy" glands in 5 women, and of these 5 only 1 was pregnant, the other 4, however, showing a definite relation to the menstrual process — 3 being premenstrual and 1 menstrual. I have frequently seen such glands in the premenstrual mucous membranes of non-pregnant women. According to Hartje, the maximum gland changes, with papillary formations, etc., are seen in about one third of premenstrual cases, the remainder showing merely the tooth-like or saw-like appearance characteristic of less advanced stages.

Stromal Changes during Menstrual Cycle.— As already stated, the stromal changes are usually less conspicuous and less constant than those seen in the glands. In a series of 50 cases, which I studied, there were 4 in which decidual modifications of the stroma cells were sufficiently marked to be conspicuous. All of these occurred among a group of 13 cases in which the glands exhibited premenstrual changes. Among these, however, was 1 in which operation was done 10 days after menstruation, so from this, it would seem that other influences than normal menstruation may perhaps be capable of producing a decidual modification of the stromal cells. At one time the decidual cell was looked upon as practically pathognomonic of pregnancy. A number of observers, notably Löfquist, have found decidual cells present to a more or less marked degree independent of pregnancy, in association with such conditions as adnexal diseases, tumors, displacements, etc. In most cases, unfortunately, the value of such observations is lessened by the failure of the authors to recognize the possible influence of menstruation in producing a decidual modification of the stroma cells.

In a few of the more recent reports, however, such as that of Goodall, this possibility seems to have been borne in mind, and it is quite probable that the stromal changes, as well as the gland changes, may be brought about by various conditions other than normal menstruation, such as inflammatory diseases, tumors, displacements, and tuberculosis. This would merely be in keeping with the biologic law that the natural result of overnutrition of tissue is overgrowth. As with the decidual cells of pregnancy, the decidua-like cells of menstruation are seen most conspicuously in the superficial compact layer of the endometrium. (Figs. 5 and 7.) They are much less characteristic of the premenstrual period than are the glandular phenomena. Like the latter, they reach their highest development just before the beginning of the menstrual period.

According to Hartje, the decidual-like cells (*decidua-ähnliche zellen*) are seen in about one third of the premenstrual cases. All stages of development are seen, from the normal stroma cells, with no protoplasm, to the typical decidual cell with its large oval nucleus surrounded by a well marked protoplasmic area. Those who maintain that there is an essential difference between the decidua-like cells of menstruation, and the genuine decidual cells of pregnancy, have not been able to define wherein the difference lies. The conclusion is forced upon us that the modified stroma cells of menstruation (*übergangszellen*) are simply different stages in a series in which the true decidual cell represents the maximum development. As Löfquist said, "All the commonly observed changes in the endometrium may be regarded as the response of the tissue to stimulation — as varying degrees of what has been called the decidual reaction."

VASCULAR CHANGES OF MENSTRUATION

So far I have said nothing as to the vascular changes in the uterus itself. The blood vessels of the uterus are enlarged and engorged with blood, and, according to the observation of Willey and others, many of the capillary fissures observed in the endometrium during menstruation disappear in the intermenstrual period. Inasmuch as menstruation is a vasomotor phenomenon, the study of the circulatory changes in the uterus is obviously of fundamental importance. Up to a few years ago the attention of investigators was directed mainly to a study of the blood supply of the endometrium. More recently, however, the muscular wall of the uterus has received much attention from this standpoint.

There are many now who believe that the endometrium plays a purely passive part in the monthly cycle, and some who look upon the menstrual bleeding as dependent upon changes in the muscular wall rather than in the endometrium itself. Whatever the truth may be as regards this process, at the time of the menses and just preceding it, the blood vessels of the endometrium are overdistended with blood and, as already stated, many new capillary fissures become apparent. It is probable that these are not newly formed, but that they become visible only when distended with blood at the time of menstruation. "The endometrium is richly supplied with arteries derived from the parenchyma. These run along the utricular glands in such a manner as to completely encircle them by capillaries. They form immediately under the epithelial coat an irregular network of wide vessels, from which the valveless veins originate, to collect in turn in the uterine and pampiniform plexuses." (Spiegelberg.) A great many years ago Tarnier stated that the menstrual hemorrhage is venous in its origin, basing this statement upon the fact that the small blood vessels of the endometrium become very much enlarged during pregnancy, and that they are then seen to belong to the venous system. He admits, however, that there may be a certain amount of arterial blood mixed in with the venous. This old view of Tarnier is interesting in the light of the recent work of Sampson. In the course of a painstaking study upon the blood supply of uterine myomata, carried out by the injection method, he concludes that the menstrual bleeding has its origin in the veins.

The question of just how the blood escapes from the blood vessels to the surface of the epithelium has been discussed for many years. Gebhard's old theory of menstruation assumed that the blood made its way out largely by rhexis, being then collected under the epithelium in the form of what he called "subepithelial hematomata." These tiny collections of blood, he stated, lift up the epithelial cells, which degenerate and thus allow the blood to break through to the surface. This description of the menstrual process is similar to that given by Heape of the corresponding process in monkeys. Most investigators, however, believe that the blood passes through the blood vessel walls by diapedesis and that there is no loss of

integrity on the part of the blood vessel walls. Specimens of the endometrium removed at the time of menstruation, of which I have studied a number, show a large quantity of blood within the blood vessels and usually a large number of red blood corpuscles outside of the blood vessel walls and in the stroma. (Fig. 6.) I have never, however, seen any indication of rupture of the blood vessel wall. While the question, therefore, has not been definitely settled, it would seem that the weight of evidence is in favor of the view that diapedesis is a much more important factor than rhexis in determining the passage of the blood elements from within the blood vessel walls.

IS UTERINE MUCOSA LOST AT MENSTRUATION?

Another question which has received a great deal of study, and which has been extensively discussed for many years, is whether or not there is any loss of epithelial tissue during menstruation — whether, in other words, the endometrium is wholly or partly cast off at the monthly periods. Some of the older views on this question have already been epitomized in the opening paragraph of this chapter. As already stated, the menstrual discharge, in addition to blood, mucus and leukocytes, is commonly stated to contain epithelial cells from the various portions of the generative tract.

In support of the view that only a small proportion of uterine epithelium is lost at the time of menstruation, may be mentioned the observations of Möricke, Strassman, Findley, Cullen, Williams, Gebhard, Mandl, Leopold and Meerdervoort. These authors consider that any loss of epithelium which may occur is more or less incidental and that it is not essential to the occurrence of the process.

Opposed to this, is the view that an extensive loss of epithelium is a characteristic of the menstrual phenomenon, and that this shedding is to be looked upon as a purely mechanical process. Among the supporters of this theory may be mentioned Engelmann, Kundrat, Marshall, Minot and others. According to Heape, a complete shedding of the uterine mucosa is the rule in the lower animals which menstruate, more particularly the monkey. It is interesting to note, also, that Heape considers that the stromal cells left behind are capable of metaplasia into a new epithelial lining. If this be true, it would offer an explanation of the remarkable rapidity with which the epithelium regenerates after each period. There has been no evidence, however, of similar metaplastic phenomena in the human uterus, and, as a matter of fact, the conception is rather incompatible with our notions of the histological separateness of epithelium and connective tissue.

Reference has already been made to the work of Schröder, who asserts that with each menstrual period there is a complete loss of the superficial or functional layer of the endometrium, followed by regeneration from the gland rests of the basal layer, which remains intact. The evidence for this view, however, is not conclusive.

From an examination of many hundreds of endometriums, including a number removed during menstruation, it seems to me that Schröder's view is an extreme one. I believe that in a very small number of instances the superficial layer of the mucosa may be cast off, perhaps in its entirety, constituting one type of menstrual cast, and associated clinically with the so-called membranous dysmenorrhea. On the other hand, in by far the largest number of cases, no epithelial loss can be determined, other than perhaps that occasioned by the lifting up of small strips by little collections of blood which are making their escape into the uterine cavity. (Fig. 6.) No doubt there are intermediate grades of tissue loss between these extremes.

In other words, no general law can be laid down as applicable to all women in this regard. In perhaps the majority, the loss of tissue at menstruation is very slight and only incidental. In a smaller number it may be larger, so that shreds or flakes of epithelium may be passed from the uterus with the menstrual discharge, while in the extreme cases, the superficial layer of the endometrium may be passed off as a menstrual cast. The entire question, however, is still a debatable one, and there is need of further work along this line.

IV

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CHAPTER V

ANATOMIC CHANGES IN OVARY DURING MENSTRUAL CYCLE, INCLUDING LIFE CYCLE OF CORPUS LUTEUM

GROSS ANATOMY OF OVARY

The ovaries are two oval bodies, situated one in each side of the pelvis. They are placed in the posterior layer of the broad ligament much as a setting is placed in a ring. They lie obliquely in the pelvis, although their position varies with such factors as the posture of the woman, the degree of distention of the bowels or bladder, etc. At their uterine extremities they are attached by the ovarian ligaments to the upper part of the corpus uteri below and behind the fallopian tubes. At the outer side the ovary is, by means of the fimbria ovarica, in contact with the fimbriated extremity of the tube, beyond which the infundibulopelvic ligament stretches out to the pelvic wall. The hilum of the ovary, along its attached surface, marks the entrance of the ovarian vessels, nerves and lymphatics.

The surface of the ovary is of a dull whitish appearance, being covered not by peritoneum but by the cuboidal celled germinal epithelium. In early life the surface of the ovary is quite smooth, but in the adult woman it is irregular and pitted, as a result of the constant repetition of follicular rupture during the sexual life of the woman. The senile ovary is shriveled and atrophic, its size being perhaps only half that of the adult ovary. Its surface presents a characteristic "peachstone" appearance.

Macroscopic Changes in Ovary as Result of Menstruation.— Little need be said on this subject, for there is no very conspicuous change in the gross appearance of the ovary during menstruation, with the exception of the fundamental phenomena concerned with the formation and development of the corpus luteum, as will be described in another connection. For the present we may simply say that, according to the modern view, the surface of the ovary exhibits a recently ruptured graafian follicle at some time during the first half of the intermenstrual period, for it is at this time that ovulation is now believed to take place. This, the earliest stage of corpus luteum formation, appears as a flattened vesicle, with a grayish yellow wall. Its inconspicuousness causes it to be overlooked in any but the most careful examination, as will be discussed later in this chapter. At a later period, and especially during the so-called premenstrual period, the surface of the ovary exhibits a gradually developing corpus luteum, reaching its maximum at the onset of menstruation.

Aside from this, the only noticeable changes which menstruation brings

about in the ovary are those referable to the increased blood supply at that period. The opaque surface does not indicate the hyperemia of the organs as readily as might a transparent peritoneal surface, but even so there is sometimes a somewhat pinkish hue at and just before the menstrual epochs.

The increase in the size of the ovaries which is generally considered to take place at this time is due partly to the development of the corpus luteum and partly to hyperemia. Incision into the ovary at this period is associated with more bleeding than at other times.

Histology of Ovary.— Microscopically, the ovary consists of a fibrous stroma, in which are found the epithelial elements which constitute

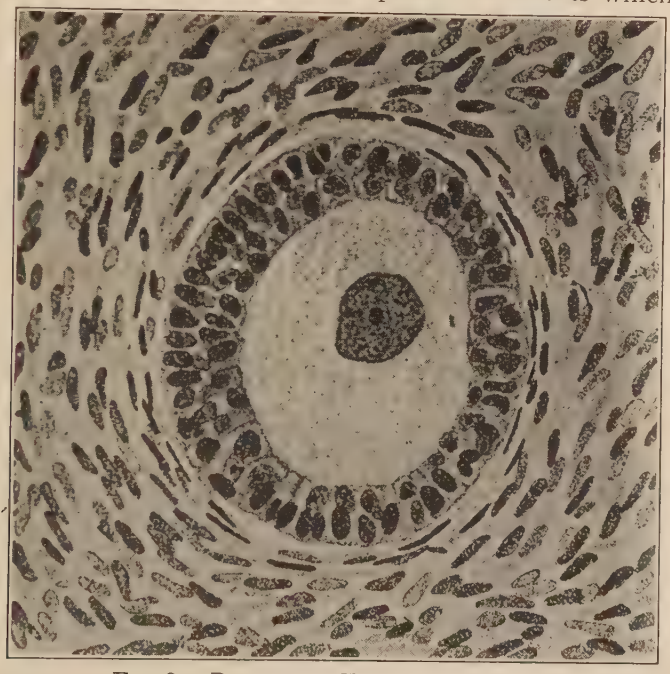

FIG. 8.— DEVELOPING FOLLICLE (Williams).

the functionating part of the organ. While some authors have suggested that the stromal tissue of the ovary is also concerned in the production of an internal secretion, the evidence for this view is inconclusive. From our present viewpoint, therefore, we may dismiss the stroma of the ovary by merely stating that it is made up of a more or less spindle celled, compact fibrous tissue (Fig. 8); that it supports the epithelial elements; and that it carries the blood vessels, lymphatics, and nerves of the ovary.

The important constituents of the ovary, from a functional viewpoint, are (1) the *follicles;* (2) the *corpora lutea;* (3) the *interstitial cells.* Embryologically, all three of these elements are believed to have a common origin in the early germ cells or oögonia (Waldeyer, von Winiwarter, Skrobansky, McElroy).

THE FOLLICLES OF THE OVARY

The Primordial Follicle.— The early stage of follicular development — the *primordial follicle* — possesses a very simple structure. It consists of the primordial ovum, or oöcyte, surrounded by a single layer of flattened epithelial cells. At a slightly later period, the latter become cuboidal in shape, while the follicle increases in size as a result of the appearance of the so-called *liquor folliculi.* (Figs. 8 and 9.)

The Graafian Follicle.— The epithelial envelope, or *membrana granulosa,* proliferates rapidly, so that it becomes several layers thick. At

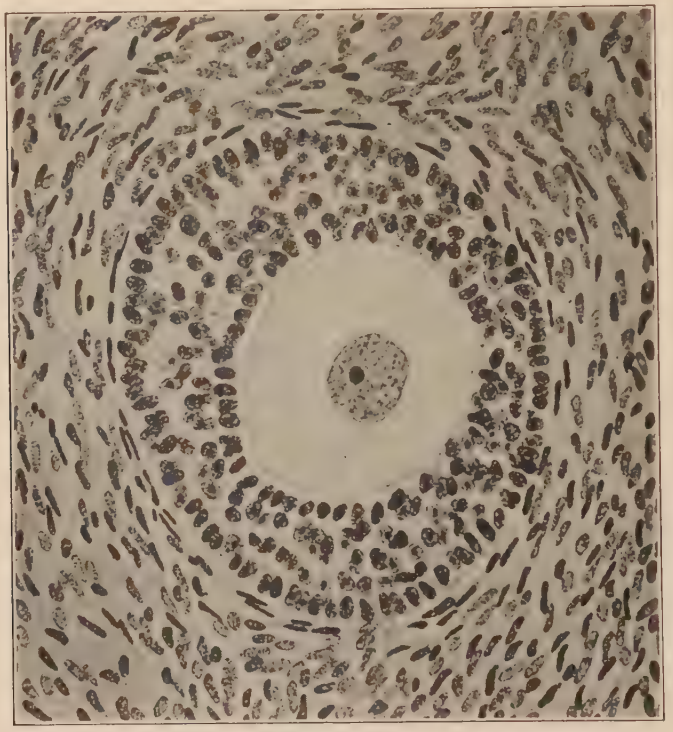

Fig. 9.— Developing Follicle; Later Stage Than Fig. 8 (Williams).

one point in the circumference of the follicle, the granulosa cells are heaped up in a peninsula-like mass which surrounds the ovum. This projection is spoken of as the *discus proligerus.* At the same time the connective tissue sheath of the follicle, the *theca folliculi,* shows a differentiation into two layers. The outer, or *theca externa,* does not differ in structure from the adjoining ovarian stroma. The inner, or *theca interna,* exhibits a slight differentiation of its cells, which become somewhat oval or polygonal and rather compactly placed. The inner layer also becomes more vascular.

In the fully developed graafian follicle, the ovum is surrounded by a layer of radially placed cells of the granulosa, the *corona radiata.* Between

the latter and the ovum is a narrow transparent zone, the *zona pellucida.* The so-called *perivitelline space* lies btweeen the zona pellucida and the ovum. The envelope of the ovum itself is the *vitelline membrane,* while its nucleus is the *germinal vesicle,* and its nucleolus the *germinal spot.* The protoplasm of the ovum, finally, consists of the *deutoplasm,* or yolk, and the protoplasm proper. (Fig. 10.)

THE CORPUS LUTEUM

General.— There is no one subject in gynecology which has received so much study in recent years as that of the histogenesis and function of

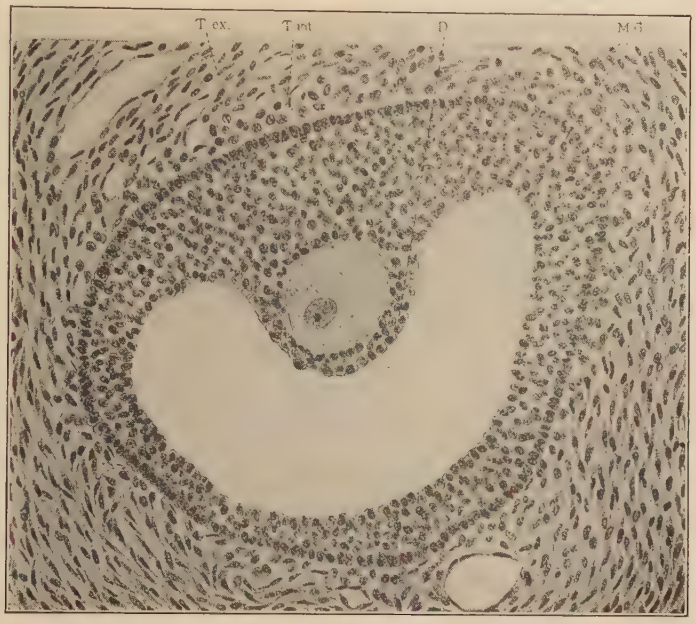

FIG. 10.— FOLLICLE APPROACHING MATURITY.

D, discus proligerus; M.G., membrana granulosa; T. ex., tunica externa; T. int., tunica interna (Williams).

the corpus luteum. To the development of our knowledge of this subject, is largely due, as a corollary, our increased knowledge of the physiology of menstruation. The remarkable series of studies, beginning with that of Fraenkel in 1903, and including the work of Robert Meyer, Ruge, Schröder, Miller, and others, have revolutionized our ideas of the physiology of menstruation, and of the relation of this process to ovulation.

Older Views as to Corpus Luteum.— Previous to the contribution of Fraenkel in 1903, the corpus luteum was commonly described as the end product of the graafian follicle. After the rupture of the latter at ovulation, there was said to be a hemorrhage into the cavity of the follicle, together with, or — according to some — preceded by, the appearance of the

so-called lutein layer. For many years there had been a controversy as to the origin of the lutein cells, some maintaining that they arise from the connective tissue cells of the theca interna, others that they are formed from the epithelial cells of the membrana granulosa. As we shall see, opinion is even now not unanimous on this point.

The later history of the corpus luteum was described by the older authors as depending upon whether or not pregnancy supervenes upon ovulation. If it does, the resulting corpus luteum — the true corpus luteum or *corpus luteum verum* — not only does not immediately retrogress, but actually and markedly increases in size up to the third or fourth month of pregnancy, after which retrograde changes appear. On the other hand, if pregnancy fails to occur, the resulting *corpus luteum spurium,* or false corpus luteum, begins to diminish in size almost at once. The blood clot becomes gradually organized, the lutein layer more and more convoluted, the cells gradually losing their pigment, until finally only a convoluted cicatricial body, the *corpus fibrosum* or *corpus albicans,* marks the site of the former graafian follicle. In the case of the corpus luteum of pregnancy, similar retrogressive changes occur, except for the long delay in their appearance. In either event, no physiological function was ascribed to the corpus luteum by the older authors.

Modern Conception of Corpus Luteum.— Although it was Fraenkel's work which gave the impetus to the study of the corpus luteum, his investigations were concerned with the physiological function of the corpus luteum rather than with its origin and structure. It is with the latter subjects that we are especially concerned in the present chapter. The epoch-making demonstration by Hitschmann and Adler that the endometrium undergoes a cyclical variation corresponding to the various phases of the menstrual cycle suggested the inquiry as to whether the corpus luteum of menstruation also passes through a series of stages corresponding to the various stages of the menstrual cycle. That this is actually the case was demonstrated by Robert Meyer in 1911, and has since then been confirmed by a number of other investigators.

In view of the frequent fallibility of the menstrual anamnesis, it seemed more scientific to fix the exact period in the menstrual period by the histological appearance of the endometrium rather than by the patient's statements. Since there is no longer any doubt of the sequence of histological changes in the endometrium, such a criterion would seem to be free from objection. Schröder believes that the exact period of the cycle at which an endometrium has been removed can, by microscopic examination, be determined within a margin of two days. It is probable that there are few who would make pretense to such diagnostic precision as this. There is no difficulty, however, in determining the stage at which the endometrium is removed — whether postmenstrual, interval, premenstrual, or menstrual — and this, after all, is the important point. (Chapter IV.)

Using the histological changes in the endometrium as a criterion, Meyer

was able to describe the development of the corpus luteum by corresponding stages, from its formation after ovulation to its ultimate fate. It is now possible to determine the stage of development of a corpus luteum from its histological appearance.

The failure of earlier observers to describe the life history of the corpus luteum was in a large measure due to the error of studying only what macroscopically were looked upon as recent corpora lutea, i. e., those structures which possess the characteristic yellow wall and which usually contain blood in their lumina. In this way the small thin walled structures, often without bloody contents, which represent the very early stages of the corpora lutea, received scant attention.

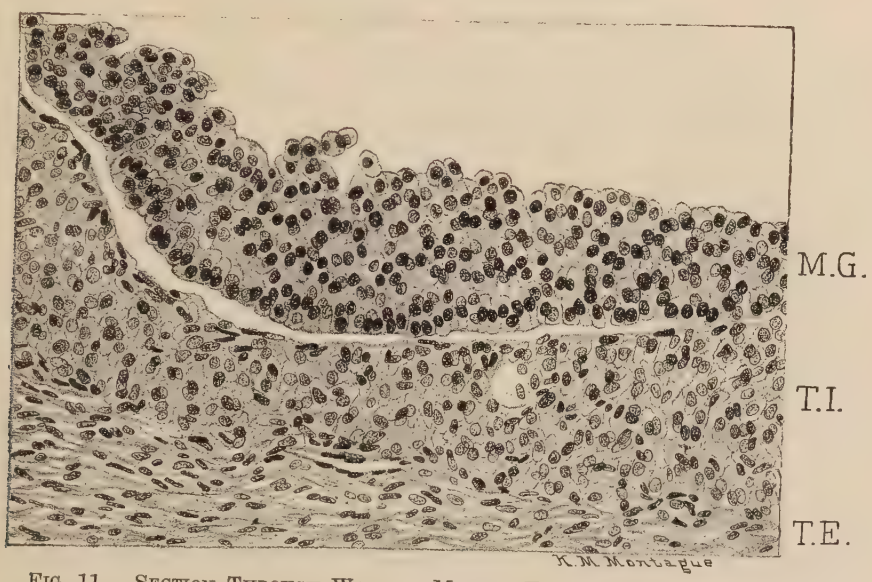

FIG. 11.— SECTION THROUGH WALL OF MATURE FOLLICLE (highly magnified). (Williams).
M.G., membrana granulosa; T.I., tunica interna; T.E., tunica externa.

Life Cycle of Corpus Luteum.— The life history of the corpus luteum may be divided into four stages: (1) the stage of proliferation; (2) the stage of vascularization; (3) the stage of maturity; (4) the stage of retrogression.

THE STAGE OF PROLIFERATION.— Preceding the rupture of the follicle certain rather characteristic changes are noted in its wall — changes which are indicative of maturation of the follicle. The cells of the theca interna become larger and clearer, gradually losing their connective tissue character, so that all grades of transition may be noted between the spindle cells of the theca externa and the polygonal cells of the theca interna. The division between these two layers is therefore not very distinct. The theca interna, on the other hand, separates itself from the membrana granulosa, which becomes much increased in thickness.

The cells of the granulosa may show mitoses and other evidences of proliferation, usually becoming cubocylindrical in shape. These changes, it may be added, are not uniform in all parts of the follicle wall. All this, it must be borne in mind, occurs before the follicle wall has ruptured, and may be looked upon as a preliminary to the more active proliferative changes characteristic of the early stages of the corpus luteum itself. (Fig. 11.)

The process of rupture of the follicle, as already stated, does not always

FIG. 12.— PORTION OF WALL OF EARLY CORPUS LUTEUM, REMOVED ON TENTH DAY OF CYCLE (low power).

mg, membrana granulosa; th, theca interna. Note the vascular line of demarcation between these two layers.

involve bleeding into the cavity of the lumen, and, as a matter of fact, bleeding is by some (Ruge) looked upon as exceptional. With the evacuation of the liquor folliculi it often happens that not only does the ovum with the "cumulus ovigerus" escape, but that here and there the inner layers of the granulosa are denuded and that perhaps even the theca interna is entirely separated in places from the granulosa. The capillaries of the theca externa and interna are widely dilated, blood elements not infrequently being found in the tissue surrounding the follicle.

The theca cells, which in the ripening follicle form a compact layer around the granulosa, are in the stage of proliferation more or less separated by the vascular dilatation, bleeding and edema, presenting a rather disorderly appearance as a result. I have elsewhere emphasized the *subgranulosal vascular wreath* which sharply marks off the theca from the granulosa. (Figs. 12 and 13.)

The size of the theca cells increases, especially because of fatty infiltration, which correspondingly diminishes their staining capacity. Meyer lays stress upon the enormous increase in the fatty content of both the granulosa cells and those of the theca. Miller denies that neutral fat is to be found in the cell layers of the young corpus luteum, while lipoid substances, on the

Fig. 13.— High Power Picture of Corpus Luteum Shown in Fig. 12. Compare with Fig. 14.

other hand, are present. Only in the stage of retrogression, he states, is neutral fat found in the corpus luteum. He further asserts that the yellow color assumed by the lutein cells is due, not to the presence of neutral fat, but to the formation or deposit of a special pigment.

The granulosa cells become more and more polygonal, take the stain less deeply, and gradually become converted into the so-called lutein cells. (Fig. 14.) This latter change takes place quite unevenly, so that at different points in the same corpus luteum may be seen clearly differentiated lutein cells and more or less unchanged granulosa cells.

Grossly, the very early corpus luteum appears as a thin walled, collapsed

vesicle on the surface of the ovary. The point of rupture may be evident, but hemorrhage into the lumen is not characteristic. The walls, however, are usually hyperemic, possibly giving the vesicle a hemorrhagic appearance. The inner surface is of a yellowish gray hue, and the wall presents only a slight degree of undulation.

The Stage of Vascularization.— This, the second stage in the development of the corpus luteum, begins with hemorrhage from the greatly dilated theca capillaries into the granulosa layer and into the lumen. At the same time endothelial cells from the vessels of the theca interna push

Fig. 14.— Wall of Early Corpus Luteum, Slightly More Advanced Than That Shown in Fig. 20 (high power).

Note the lutein-like change of granulosa cells, and beginning retrogression of theca cells.

between the granulosa cells up to the lumen of the corpus and form new capillaries in the epithelial zone. This process of vascularization proceeds quite rapidly, and hence is overlooked by a good many investigators. Only rarely, as in the case pictured by Meyer, does the beginning of the process of vascularization come under observation; usually the entire granulosa has been permeated with blood when the corpus luteum is obtained for study. In the outer layer of the epithelial zone the blood is contained in the vessels, while toward the cavity it may lie free between the epithelial cells. (Fig. 15.)

While vascularization is the most important and the most conspicuous feature of this stage, changes in the epithelium are also noted. The cells

become more distinctly lutein-like, the epithelial zone being quite clearly marked off from the theca interna.

The endothelial cells during the process of vascularization often push beyond the inner border of the lutein cells into the extravasated blood in the lumen. Connective tissue cells also not infrequently penetrate the epithelium and invade the lumen. The inner margin of the lutein layer is thereby given

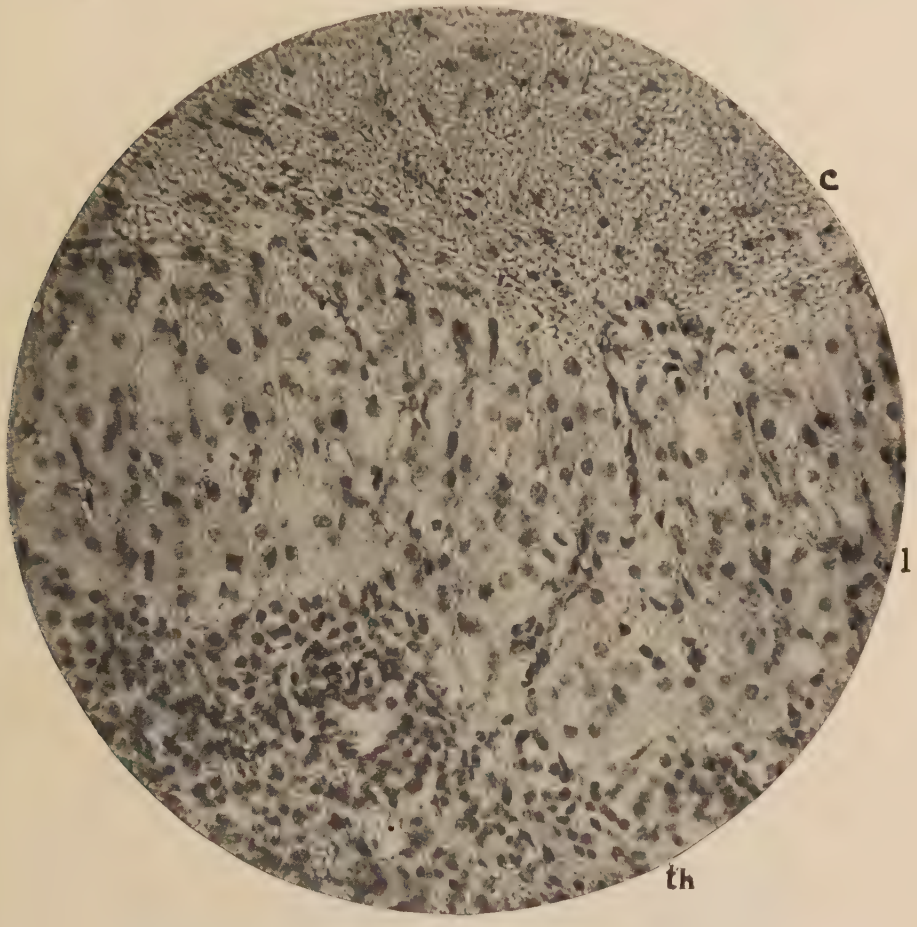

FIG. 15.— WALL OF CORPUS LUTEUM IN STAGE OF EARLY VASCULARIZATION, SIXTEENTH DAY (high power).

Blood vessels from the theca are pushing into the granulosa layer (l), which now possesses definite lutein characteristics. The theca cells (th) have lost their fat and are retrogressing. Note the beginning invasion of the blood in the cavity (c) by endothelial cells.

a very irregular appearance. Gradually there is developed on this inner border a layer of connective tissue cells and blood vessels which forms a sharp dividing line between the lutein cells and the blood within the lumen.

In this stage the wall of the corpus luteum becomes bright yellow in color and takes on a moderately wavy outline. Blood now becomes apparent in

the lumen, usually as a narrow zone along the inner margin of the lutein layer, although sometimes the lumen is practically filled.

The Stage of Maturity.— The completion of vascularization and the formation of the dividing membrane between the lutein layer and the contents of the lumen indicate that the corpus luteum has reached the point of maturity. (Fig. 16.) From now on it functionates as a ductless gland, giving off its secretion into the blood stream, instead of into the lumen. The lutein cells become larger and more or less polygonal. The lutein zone as a whole assumes a more and more undulating outline, owing to the rapid

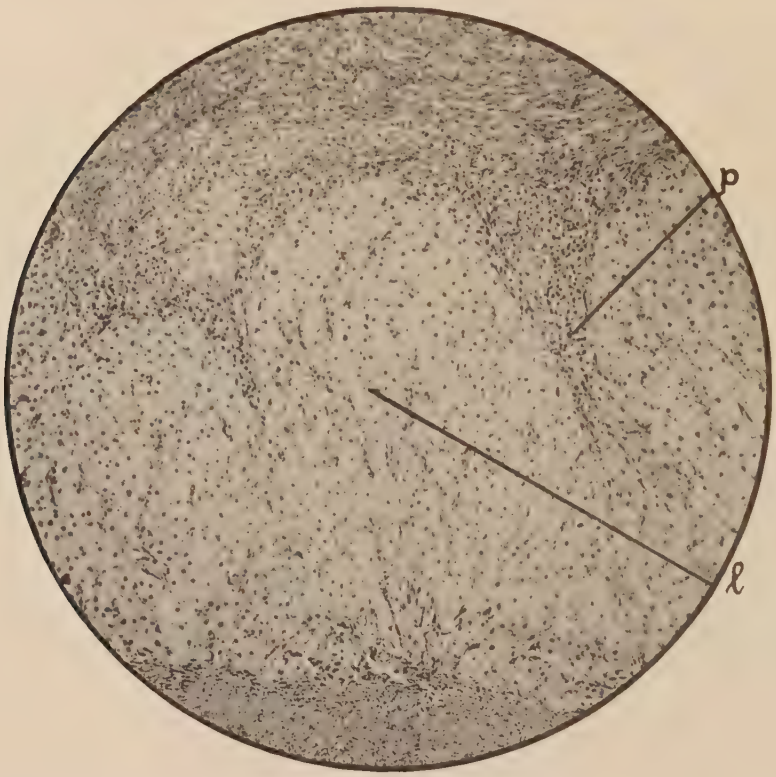

Fig. 16.— Wall of Mature Corpus Luteum, Twenty-seventh Day (low power), showing lutein (l) and paralutein (p) cells. The latter are found in the wedge-like septa.

relative increase in the cells as compared to the surrounding tissue. Not infrequently the large size and alveolar arrangement of the theca cells — the so-called "paralutein" cells — suggests an internal secretory function. (Fig. 17.)

In this stage the corpus luteum appears as a conspicuous yellow-walled structure, varying usually from 1 to 2 cm. in diameter. The lutein layer is very undulating, and the position of the corpus luteum is usually marked on the surface of the ovary by a dark reddish, hemorrhagic mound. (Fig. 18.)

The Stage of Retrogression.— This stage is characterized by a

shrivelling of the lutein layer as a result of the development of connective tissue fibrils between the cells. The process of organization in the contents of the lumen advances progressively, while the theca, already less distinct, disappears entirely in this stage. These retrogressive changes do not proceed with the same degree of rapidity in all cases. The theca cells may still be large and numerous in the stage of retrogression of the corpus

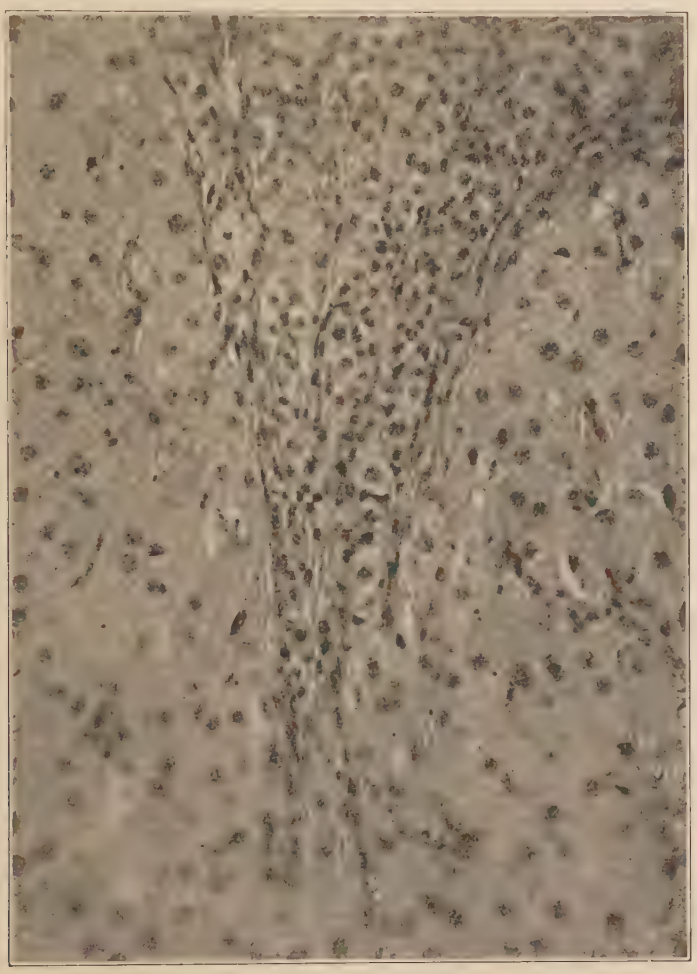

FIG. 17.— CONTRAST BETWEEN LUTEIN AND PARALUTEIN CELLS, NEAR TOP OF SEPTUM SHOWN AT p IN FIG. 16 (high power).

luteum, while in other cases they are quite sparse even in the stage of maturity. In the same way organization of the blood in the lumen may be quite advanced in the beginning of the stage of maturity, although it does not become marked until the lutein cells show much retrogression.

There is no sharp dividing line between the stage of maturity and that of retrogression. One blends gradually into the other. I have often found it

impossible to distinguish corpora lutea removed just after menstruation from those removed just before, even though retrogressive changes are said to set in with the onset of menstruation. The individual variation in the rapidity of retrogression is illustrated by the fact that in some cases four or five well marked corpora lutea, in various stages of retrogression, may be observed, while in others only one is noted.

There has been much discussion as to the significance of fatty changes in the lutein cells. This is a prominent, though probably not a characteristic feature of this stage. Together with this, it will be seen that the connective tissue trabeculae ramify more boldly through the lutein zone, while organization of the contents becomes more advanced, the process being due to

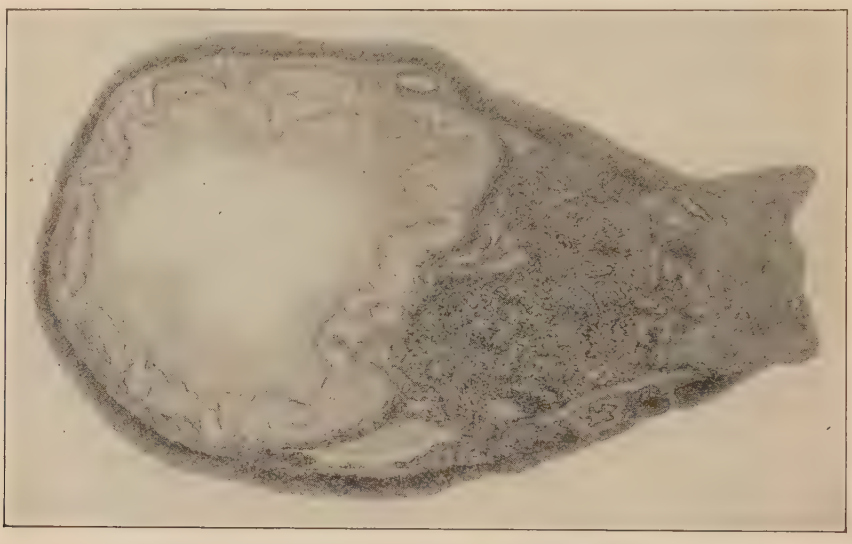

FIG. 18.— A TRANSVERSE SECTION OF THE OVARY, ABOUT THREE TIMES THE NORMAL SIZE, SHOWING A LARGE, MATURE CORPUS LUTEUM.

It embraces about half the cross section of the ovary. Note the festooned lutein layer, and the narrow zone of blood just within it.

invasion by the endothelial and connective tissue cells of the lutein layer. The central core of organizing tissue on the inner side and the theca at the outside are thus connected by a gradually shrinking fibrous meshwork, showing more and more evidence of hyaline change. Little by little the lutein cells are crushed out, until finally, in the *corpus albicans,* there remains only the shrunken and hyalinized outline of the wavy lutein layer, surrounding the central core of well formed connective tissue. The sharpness of outline of the hyalinized lutein layer, both internally and externally, is worthy of note, indicating the remarkable special reaction of the lutein cell, even after its death. (Figs. 19 and 20.)

Chronological Relation of Corpus Luteum Cycle to Menstrual and Endometrial Cycles.— The study of a large number of corpora lutea

with reference to the histological appearance of the endometrium at different stages of the menstrual cycle shows that a very definite relation exists between the two. This relation is confirmed by a study of the menstrual histories in such cases. Meyer and Ruge state that the stage of proliferation begins at any time between the first and the fourteenth days of the menstrual cycle, the first day of menstruation being considered, of course, as the beginning of the cycle of twenty-eight days. This is another way of saying that ovulation occurs at some time between the first and fourteenth days of the cycle.

FIG. 19.— CORPUS LUTEUM SHOWING BEGINNING OF RETROGRESSION (low power).

Miller, on the other hand, places the time of follicular rupture at about the eighteenth day of the cycle, i. e., about nine days before menstruation. Schröder, again, on the basis of a large number of observations, states that ovulation occurs between the fourteenth and sixteenth days of the cycle. My own investigations, which include the study of a large amount of material, would indicate that while the time of ovulation differs in different women, it can usually be placed between the fifth and fourteenth days of the cycle.

The stage of vascularization in the corpus luteum corresponds to the latter portion of the interval stage in the endometrial cycle, while the full development of the corpus luteum, i. e., the stage of maturity, is associated with the hypertrophic and secretory changes so characteristic of the pre-

menstrual period in the uterine mucosa. Finally, the onset of menstruation initiates the retrogressive stage in the cycle of the corpus luteum. This subject, however, is discussed more fully in Chapter XVI.

The time relation existing between menstruation, the histological appear-

FIG. 20.— A CORPUS ALBICANS.

Note the sharp outline of the hyalinized, festooned, lutein zone.

ance of the endometrium, and the stage of development of the corpus luteum is concisely summed up by Schröder somewhat as follows:

First Stage. 15th to 20th day of menstrual cycle.— Endometrium shows midinterval or late interval picture. Corpus luteum is in its earliest stage of development. Granulosa cells still small, but gradually becoming larger. Increasing folding of epithelial layer is noted, with numerous red blood corpuscles between the cells. The inner boundary of the granulosa zone is indistinct. The formation of new capillaries is beginning. The cells of the theca interna are large, but gradually become smaller.

Second Stage. 18th to 25th day of menstrual cycle.— Endometrium shows premenstrual picture in its earlier stages. Corpus luteum ripe (stage of vascularization). Granulosa cells broad and large, the epithelial zone being markedly convoluted. Fine fibrils with capillaries traverse it, usually in a radial manner. Delicate but quite distinct connective tissue layer on inner margin of epithelial layer. Theca interna cells small.

Third Stage. 24th to 28th day of menstrual cycle.— Endometrium shows changes of end of premenstrual period. Corpus luteum completely formed and entirely organized. Granulosa as in second stage. Fibrils and capillaries more numerous, with numerous anastomoses of latter. Well defined limiting membrane of connective tissue at inner margin of lutein cells.

Fourth Stage. 1st to 14th day of menstrual cycle.— Endometrium shows postmenstrual and early interval change. Corpus luteum in retrogression. Granulosa cells shriveling up, interspersed with increasing fibrillary connective tissue growth. Connective tissue membrane at inner margin of granulosa thickened, and advancing organization of lumen contents. Theca interna quite distinct peripherally, its cells being clear and well formed.

Comparison of Corpus Luteum of Menstruation and Corpus Luteum of Pregnancy.— Practically the only difference described by the older authors between these two structures, the *corpus luteum spurium* (*menstruationis*), or false corpus luteum, and the *corpus luteum verum* (*graviditatis*), or true corpus luteum, lay in the longer life of the latter. Even this was ascribed to extrinsic conditions, especially the pelvic hyperemia associated with pregnancy.

Many of the more recent authors, such as Ravano, Hegar and Wolz, describe nó essential difference between the two structures, other than the difference in the periods during which they persist. Such an opinion was not surprising in the days when the corpus luteum was looked upon only as an end product of the graafian follicle, but it scarcely seems tenable in the light of the present day belief in the rôle of the corpus luteum as a ductless gland which is important both for menstruation and for pregnancy.

It was Aschoff who first asserted that a point of differentiation between the two was the usual absence of bleeding in the corpus luteum of pregnancy. He believed that ovulation takes place in the intermenstrual periods, and that the hemorrhage in the lumen of the corpus luteum of menstruation is due to the hyperemia of the menstrual process.

Mention has already been made of the work of Miller, who found colloid material in the lutein cells of the true corpus luteum, and emphasized the importance of this finding for purposes of differentiation.

The most complete study of this question, however, is the recent one by Marcotty, based on a material consisting of 26 corpora lutea of pregnancy, 2 corpora lutea removed during the puerperium, and 14 corpora lutea of menstruation.

Marcotty found, first of all, that the curve of blood pigment present in the corpus luteum alternates with the menstruation curve, having its beginning in the middle of the intermenstrual period. He agrees with Meyer that hemorrhage in the corpus luteum is normally present, even before the onset of the menstrual period, and that it is therefore due to a rupture of the thin walled vessels found in the stage of vascularization, under the influence of the increased blood pressure in the pelvic circulation. The influence of the menstrual congestion itself is manifested by a renewed bleeding at the time of the period.

Fig. 21.— Corpus Luteum in a Case of Early Pregnancy (low power), showing lutein cells (l), paralutein cells (p), and organization of contents (c).

In the corpus luteum of pregnancy, on the other hand, the hemorrhage due directly to the menstrual influence is of course absent, while that associated with the process of vascularization is not constant, apparently owing to different conditions of blood pressure and blood distribution.

The size of the true corpus luteum before its retrogression begins exceeds the greatest size of the false corpus. Up to perhaps the second month this larger size is due to the hypertrophy of the granulosa layer and the development of the lutein zone, after that to the development of the central core.

In the corpus luteum of pregnancy, moreover, the connective tissue membrane between the lumen contents and the lutein layer is much more marked than in the corpus luteum of menstruation. (Fig. 21.) The differences between the two structures are epitomized by Marcotty in tabular form, as follows:

CORPUS LUTEUM MENSTRUATIONIS

	Before menstruation.	*After menstruation.*
Blood.	nfrequent, small amount.	regularly, abundant.
Blood pigment.	little.	much.
Fat.	little, chiefly in theca.	much, principally in granulosa.
Colloid.	absent.	absent.
Calcium.	absent.	absent.
Size of organ.	increasing to menstruation,	then decreasing.
Size of cavity.	usually small.	organized.
Connective tissue covering.	slight.	well defined.
Size of granulosa cells.	average.	atrophic.
Theca cells.	conspicuously present.	in diminishing number.
Connective tissue framework and blood vessels.	slight.	marked.

CORPUS LUTEUM GRAVIDITATIS

	1st half	*2nd half*
Blood.	usually not present.	
Pigment.	except perhaps traces.	
Fat.	very little	more toward end
Colloid.	frequent, abundant	less frequent, less abundant.
Calcium.	absent	rather frequent.
Size of organ.	larger than corpus luteum of menstruation.	smaller than in first half.
Size of cavity.	large, cystic.	smaller, more frequently solid.
Connective tissue.	very well marked.	well marked.
Size of granulosa cells.	larger than average.	smaller than average.
Theca cells.	almost always present, but owing to flattening not conspicuous.	gradually disappearing.
Connective tissue framework and blood vessels.	fairly well marked.	well marked.

ORIGIN OF LUTEIN CELLS

No subject concerned with the corpus luteum has been the source of more study and discussion than the origin and nature of the lutein cells. An extensive literature has developed on this subject. Only a brief summary of this interesting question can be included here.

Two Principal Theories.— There are two principal views as to the origin of the lutein cells. According to one of these the lutein cells are derived from the connective tissue cells of the theca interna, and according to the other they have their origin in the epithelial cells of the membrana granulosa. The first of these was supported by von Bär, the discoverer of the human ovum, and since then by His, von Kölliker, Spiegelberg, Paladino, Schottländer, Clark, Nagel and many others. On the other hand, the theory of the epithelial genesis of the lutein cells has found able supporters in Bischoff, Pflüger, Call and Exner, Schulin, Waldeyer, Sobotta and others. The latter theory, moreover, is favored by most of the modern German school of investigators who have contributed so much to our knowledge of the corpus luteum (Meyer, Ruge, Schröder, etc.).

Origin of Lutein Cells in Lower Animals.— The question of the origin of the lutein cells in the lower animals has been quite conclusively settled by the exhaustive researches of Sobotta on rabbits, guinea pigs, mice, and other mammals. Sobotta's studies indicate that in the lower animals, at least, it is from the epithelial cells of the membrana granulosa that the lutein cells are derived.

Theory of Origin from Connective Tissue.— The view that the lutein cells have a connective tissue origin, as Williams says, is based upon two principal facts: first, that the cells of the theca interna exhibit marked changes immediately after the rupture of the follicle; and second, that degenerative changes are noted in the cells of the granulosa, which, as a matter of fact, is in large part cast off with the ovum. The changes in the theca consist in the appearance of mitoses and other evidences of proliferation, the cells becoming larger and assuming an epithelioid appearance. This is noted even in the earlier stages of follicular development. The yellow color of the lutein cell is due to the deposit of a special pigment. The fact that "the lutein cells first appear in the theca would argue against their derivation from the membrana granulosa, but even more so the fact that they are separated from it by a definite barrier of unchanged connective tissue, the upper layer of which forms the basement membrane of the follicle" (Williams).

Theory of Epithelial Origin of Lutein Cells.— As for the evidence in favor of the epithelial origin of the lutein cells mention may first be made of the work of Sobotta, already alluded to. Although his studies were made entirely upon lower animals, some of his results are without question applicable to human beings. Sobotta's work has been confirmed on many types of mammalian animals by Honoré, Cohn, Bonnet, Van der Stricht, Corner,

Marshall and others. Certainly, speaking from analogy, one would expect that in human beings also the lutein cell is of epithelial origin.

Arguing against a connective origin of the cells, Sobotta shows that the granulosa cells do not undergo degeneration, and that as a matter of fact they exhibit signs of active proliferative activity, and that there is a gradual growth of connective tissue fibrils and capillaries from the theca folliculi pushing over into the membrana granulosa.

The development of actual lutein cells from the theca interna of atretic follicles is denied by Schröder and others, in spite of the similarity in appearance of cells arising from this source to genuine lutein cells. This point is emphasized in the classification given by Cohn of lutein cells, i. e., (1) granulosa lutein cells; (2) theca lutein cells; and (3) stroma lutein cells.

The recent exhaustive studies of Miller also bring much evidence in favor of the epithelial genesis of the lutein cells. By careful methods of staining he concludes that the finding of colloid droplets in the lutein cells of the corpus luteum of pregnancy and the absence of colloid from the theca interna lutein cells proves the epithelial origin of the former, inasmuch as colloid is just as distinctive of epithelial tissue as hyalin is of connective tissue.

The principal obstacle to a complete study of the life history of the corpus luteum, and therefore of the origin of the lutein cells, has been the rapidity with which the early changes take place. Sobotta, for example, states that the structure of the human corpus luteum is complete about eight days after the rupture of the follicle. The finding of a very early corpus luteum, say only a few hours old, must therefore be a very rare occurrence. Such a structure would throw much light on the question we are now discussing. Interest attaches, especially, to the study of such early corpora lutea. The first reliable description of such a structure was given by Robert Meyer, who thus supplied the "missing link" between the granulosa cell and the lutein cell. His description of an actual transformation of granulosa cells into lutein cells, if sufficiently confirmed by later studies, would make the evidence of an epithelial origin of the lutein cells incontrovertible. I believe that this evidence is furnished by the results of a study of five early corpora lutea by myself, as reported in a recent paper.

All of the five specimens were alike in the very important particular that in all of them the epithelial cells of the granulosa were, to say the least, quite intact. This fact is of prime importance in the consideration of the origin of the lutein cells. One of the strongest arguments against the epithelial origin of these cells has been the alleged degeneration and disappearance of the membrana granulosa after rupture of the follicle. In each of my five specimens, however, the epithelium was well preserved. Moreover, in two of them it exhibited definite signs of lutein-like transformation. This I look on as a vital point — *the* vital point — in connection with the question of the origin of the lutein cell. If we can demonstrate in human beings, as Sobotta seems to have shown in lower animals, that there is a

direct transformation of the granulosa cell into the lutein cell, the problem is solved. I believe that Figures 12, 13, and 14 illustrate such a beginning transition of the granulosa cell to the lutein cell. It will be noted that this transformation is already well under way before there is any evidence of vascular invasion of the granulosa layer, and that as the granulosa cells assume lutein characteristics, the cells of the theca become less conspicuous, giving up much of their fatty content. This may be observed from a comparison of Figures 12 and 14. From this it may be inferred that the theca cells, with their rich fatty content, fulfil an important nutritive function, as Meyer has suggested. The gradual retrogression of the theca cells, moreover, is another indication that it is not they that are to be transformed into lutein cells.

Present Status of Question.— Weighing carefully the evidence in favor of each of the two theories, as to the origin of the lutein cells, it would seem difficult to avoid the conclusion that the theory of epithelial origin, from the cells of the granulosa, has been fairly well established. The question is still a live one, however, and there is need of further investigation. The great desideratum at present is the securing of many more early corpora lutea, so that all stages may be studied in the conversion of granulosa cells into lutein cells. Evidence of this sort is much more valuable than any that can be obtained from the study of the mature corpus luteum.

THE INTERSTITIAL CELLS OF THE OVARY

General.— The advance in our knowledge of the relation of the ovaries to the entire organism, through the medium of the internal secretions, has given a strong impetus to histological studies of the ovary. Among other results of such studies may be mentioned the description of the so-called interstitial glands of the ovary. It has long been known that the ovaries of many of the lower animals contain cells which are analogous to the so-called interstitial cells of Leydig in the testicle.

Like the latter cells, the interstitial cells of the ovary are apparently of connective tissue origin, being placed interstitially among the connective tissue, and having no connection with the reproductive cell, the ovum. These cells had been described as existing in the ovaries of lower animals by Pflüger as far back as 1863. Various names were applied to them by the older writers, such as " wandering cells," " plasma cells," " körnchenzellen," etc. Numerous studies of these elements, as existing in the ovaries of lower animals, have been made by Schröen, His, Waldeyer, Born, Tourneux and others.

It is Limon and Bouin, however, who deserve the credit for recognizing the glandular nature of these cells and their probable function in giving off an internal secretion. These authors bestowed upon these structures the name of " glandes interstitielles de l'ovaire," Bouin having used this name in describing the interstitial cells in the ovary of the frog (rana temporia).

Interstitial Cells in Ovaries of Lower Animals.— The studies of Limon upon various lower animals — rabbits, rats, mice, guinea pigs, bats, moles, and hedgehogs — led him to describe, in addition to the follicles and corpora lutea, a third epithelial structure, consisting mainly of polygonal epithelioid cells, with an average diameter of 12 to 15 microns. The nuclei of these cells are round, with a diameter of 4 to 6 microns, while the protoplasm contains many small vacuoles, staining black with osmic acid. These cells are usually arranged either in rather compact clumps or strands several cells thick, or in small hollow collections whose cleft-like lumina are filled with fine connective tissue. Sometimes, on the other hand, the cells lie scattered in the ovarian stroma without any very definite arrangement. The

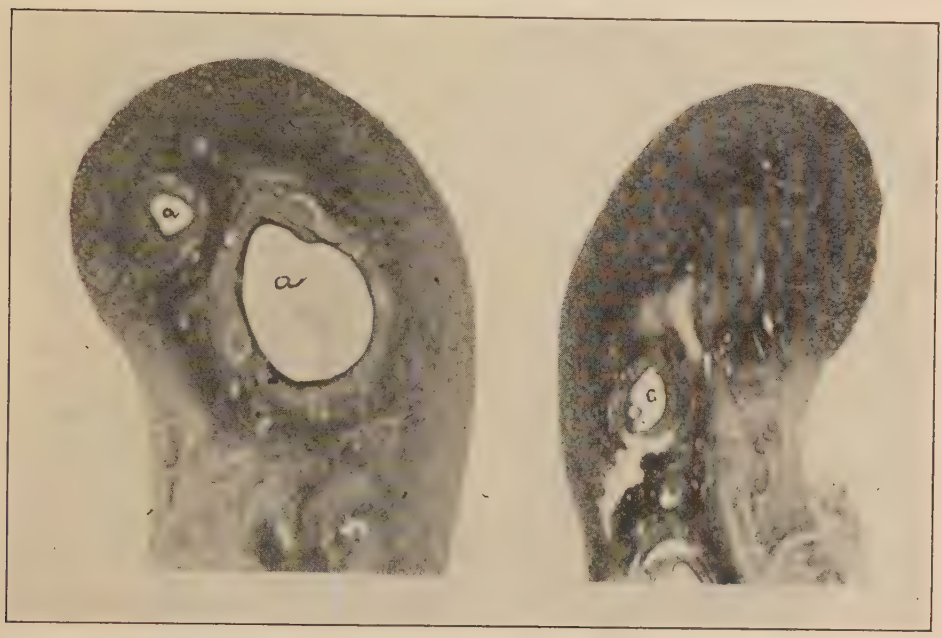

FIG. 22.— SECTIONS OF OVARY OF INFANT 2 DAYS OLD, showing cystic atretic follicles (a) and maturing graafian follicles (G). (Very low power).

interstitial cells are perhaps best studied in the ovaries of rabbits, in which they are abundant.

L. Fraenkel has also studied the question of the occurrence and morphology of the interstitial gland in the ovaries of as many as forty-five different varieties of animals, belonging to the orders of Marsupialia, Ungulata, Carnivora, Rodentia, Insectivora, Chiroptera and Simiidae. In addition, from a study of a large number of human ovaries, he concludes that interstitial gland tissue is present only in traces in the ovaries of adult women, and that it bears little resemblance to the corresponding tissue in the lower animals.

Interstitial Cells in Human Ovary.— Fraenkel's opinion is opposed to that of Wallart, who has perhaps studied the subject, from the standpoint

of the human ovary, more exhaustively than any other author. After a large number of observations, Wallart is convinced that interstitial gland tissue exists in human ovaries, that it is most highly developed and most abundant in the earlier years of life, up to the age of puberty, that it is much increased during pregnancy, and also to a less extent during menstruation, and that the formation of the tissue ceases after the climacterium. The

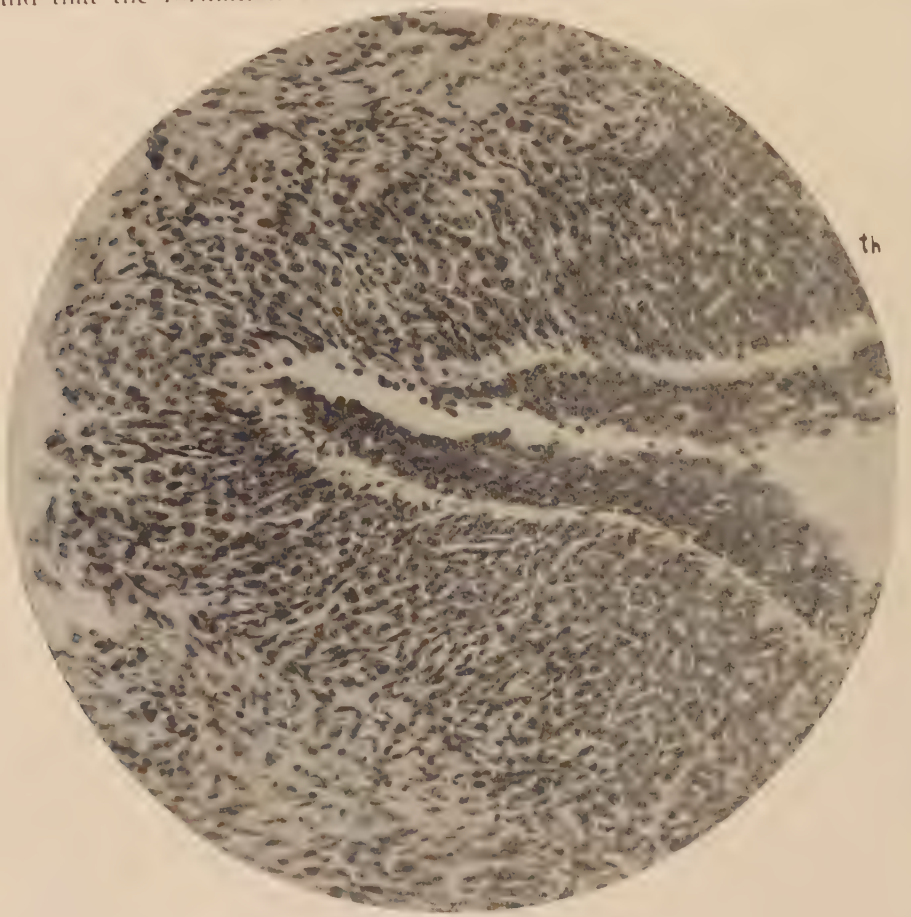

FIG. 23.— CORNER OF ATRETIC FOLLICLE, showing degeneration of epithelium (E), and the alveolar grouping of the theca cells (th).

The two layers are separated by the refractile "glashaut," described first by Grohe. (High power.)

work of Seitz confirms the statements made by Wallart on the occurrence of interstitial cells during pregnancy, while Cohn, Meyer and others of the modern German school arrive at results in substantial agreement with those of Wallart. In human beings, the cells corresponding to the interstitial cells found in the ovaries of certain lower animals are formed from the cells of the theca interna of atretic follicles. These cells become large and

epithelioid in appearance, while the protoplasm undergoes a fatty change. In the most marked cases these modified theca cells form a broad zone of rather alveolar pattern, surrounding the atretic follicle. These changes are to be found most characteristically in the ovaries of pregnant women.

Origin of Interstitial Cells from Walls of Atretic Follicle.— The study of the interstitial cells in human ovaries is intimately bound up with the study of the process spoken of as follicular atresia, for it is the latter process which now seems to be quite generally accepted as responsible for the production of the interstitial cells.

Only a very small percentage of the follicles in the ovary attain maturity, with the discharge of ova and the development of corpora lutea. The

Fig. 24.— Cystic Atretic Follicle Undergoing Obliteration (above and to left).

great number sooner or later exhibit the phenomenon of atresia, which is characterized by degeneration of the ovum and of the epithelial cells of the granulosa. I shall not here discuss the influence which brings about this arrest in the development of the follicles, except to say that it seems to emanate from the discharged ovum. The cyst-like cavities resulting from atresia are found in practically all ovaries during the reproductive period, and not infrequently even in the ovaries of fetuses and young children. (Fig. 22.) When present in excessive number, they give rise to the well known fibrocystic disease of the ovary. The later history of the cystic atresic follicle is a gradual process of obliteration. In other words, the two varieties of atresia folliculi described by Seitz, the cystic and oblit-

erative, are in reality only different stages of the same process. (Fig. 24.)

The theca cells of the atretic follicle exhibit a striking change during pregnancy, giving rise to the so-called interstitial cells, which are thus seen to be of connective tissue origin.

The retrogression of the atretic follicle gives rise to a terminal structure somewhat different from that left after the life history of the corpus luteum is run, i. e., the *corpus fibrosum*. The studies of Wolz lead her to believe that the theca lutein cells, i. e., the interstitial cells, can never become converted into the lutein cells of a corpus luteum, nor can they, after fulfilling their own function, be converted into stromal connective tissue cells. They disappear altogether, their site being marked by the hyalin connective tissue of the corpus fibrosum.

V

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CHAPTER VI

HISTORICAL SKETCH OF OLDER THEORIES OF MENSTRUATION

Introduction.— Innumerable hypotheses have from time to time been offered to explain the occurrence of menstruation. A few of the earliest views on the subject have already been described in Chapter I. The older theories of menstruation now possess only a historic interest, but a brief review of the more important among them may be of interest as illustrating the evolution of our knowledge of the cause, nature, and mechanism of the menstrual process.

The Earliest Theories of Menstruation.— The three factors variously considered by the earliest writers to be responsible for the occurrence of the menstrual flow were (1) the influence of the moon, (2) the action of a "ferment" circulating in the blood, (3) the condition of plethora, which was held to exist in all women.

The Theory of Lunar Influence.— The so-called lunar theory has already been discussed in Chapter I.

The Ferment Theory — The "Fervor Uterinus" of Democritus. — Not a few of the early writers, to quote Freind, "deduce the course of the Menstrua from a certain Ferment; which indeed, though it be clouded by another word, is the same as the Fervor Uterinus of Democritus. They imagine indeed the monthly Colluvies to be purged off at the Uterus by the means of a Ferment, which de Graaf thinks diffused thro' the whole Mass of Blood, but Boyle asserts it to be peculiar to the Uterus. They both pretend that this Ferment is seated in some certain Salts, which by their Motion so exagitate the Mass of Blood, that at some certain Season, namely, every Month, it is thrown into a vehement Effervescence, and seeks a Passage by the uterine Vessels."

The Plethora Theory of Galen.— Galen, in his *Book of Bleeding against Erasistratus,* attributes the menstrual discharge to a condition of plethora. "Does not" he says "Nature herself cause an Evacuation in all Women, by throwing forth every Month the superfluous Blood? I imagine that the Female Sex, inasmuch as they heap up a great quantity of Humors, by living continually at home, and not being used to hard Labour, or exposed to the Sun, should receive a discharge of this Fulness, as a remedy given by Nature." Freind, like many others of his era, was a firm believer in this doctrine, and he devoted many pages of his "Emmenologia" to ponderous arguments in its behalf. He shows very clearly, to his own

satisfaction at least, that plethora exists in all women, and that this is in large measure due to the fact that perspiration is less in women. It is of interest to note that this plethora theory of Galen held sway among medical men even up to about the middle of the last century.

The Theory of Pflüger.— The beginning of our modern knowledge of the subject may be traced from the discovery by Negrier, in 1832, that the ovary is in some way associated with the occurrence of menstruation, although it was not until 1840 that Gendrin asserted the dependence of menstruation upon ovulation. The best known of the more modern theories of menstruation was that of Pflüger, who believed that the occurrence of menstruation is the direct result of the ripening of a graafian follicle at that time. The gradual distention of the substance of the ovary, as the follicle grows larger and larger, sets up an irritation of the ovarian nerve. The reflex irritation thus brought about is exerted especially upon the spermatic or utero-ovarian arteries, so that they exhibit an active dilatation. This produces pelvic congestion and an increased blood pressure, together with the other symptoms associated with menstruation. As a result of the hyperemia in the pelvis, there occurs a thickening of the endometrium, epithelial and gland proliferation, and finally rupture of the blood vessels with escape of the blood. An effort to substantiate this theory was made by Strassman, who endeavored to simulate ripening of the follicle by injecting sterile water into the substance of the ovary. His work, however, was not by any means conclusive. Although the theory of Pflüger retained much of its popularity up to quite recent years, it has now been generally discarded.

The " Tubal Nerve " of Tait.— The same may be said of the theory of Lawson Tait, who attributed menstruation to the presence of the so-called tubal nerve. He stated that removal of the tubes, the ovary being left behind, is followed in ninety-five per cent of the cases by cessation of the menses. This is obviously incorrect, and the theory of Tait now possesses only a historic interest.

The Influence of the Vertical Position in Causing Menstruation.— An interesting and quite elaborate theory advanced by Johnstone, which was in high favor for some years, is that the occurrence of menstruation in human beings is explainable by the erect position, in contradistinction to the horizontal position of most of the lower animals. No horizontal animals menstruate; all vertical animals do. The os uteri of the horizontal animal points upward and the other end of the uterus points downward. This makes it impossible for such a uterus to drain itself through the cervix, as is the case in the vertical animal. Among other things Johnstone believed that the lymphatics of the normal endometrium in animals are not sufficiently developed to absorb the decidua of menstruation, which must, therefore, be expelled into the vagina like the decidua of pregnancy. Johnstone states that in the ordinary acceptation of the term the endometrium above the internal os is not a mucous membrane, but that it belongs to the so-called

adenoid tissues, and that menstruation is for it exactly what the lymph stream is to lymph glands and the blood stream for the spleen. He agrees with those who do not believe that ovulation and menstruation are dependent upon each other, nor does he believe that menstruation in the human female is either homologous or analogous to the estrus of the lower animals. Being convinced of the adenoid nature of the endometrium, he states that "the tissue then belongs to that class of organs whose function it is to replace the organic waste and that it ought to be ranked with the spleen and thymus gland instead of the vagina and bladder."

Menstruation as a Result of the Sexual Appetite.— The theory of Beigel and others was that "ovulation and menstruation are in no sense dependent one on the other, but are both the result of the sexual appetite." Of the arguments against this theory may be stated: Firstly, menstruation is periodic in occurrence, sexual feeling is not; secondly, congenital absence of the ovary necessitates absence of menstruation, and yet sexual feeling may remain; thirdly, removal of the ovaries ordinarily is followed by cessation of menstruation, while sexual feeling often remains undiminished.

"Women Menstruate Because They Do Not Conceive." — The view originally put forth by Sigismund, and later adopted by His, was that the growth stage of menstruation prepares a bed for the fertilized ovum and that the degeneration stage of menstruation is to be looked upon as a retrogression, taking place because such an ovum is not present. This idea was expressed by Powers in the well known dictum, "women menstruate because they do not conceive." It is evident that, according to this theory, ovulation must take place prior to menstruation — a view which, as we shall see, is in harmony with our modern theory. Somewhat different is the theory of Geddes and Thomson, according to which "the process is viewed as a kind of cleansing process of the uterus for the reception of the ovum, whereby the latter during the healing process can be attached safely to the uterine wall."

Menstruation an "Unnatural Process."— A rather grotesque view, put forth in 1876 by the late Dr. A. F. A. King, of Washington, was to the effect that the process of menstruation is not a physiological one, being the result, as he says, of an interference with nature, of a thwarting of her designs, and a violation of her laws. He states that menstruation is a hemorrhage, being attended with the rupture of the blood vessels. Blood vessels are not made to rupture, and no hemorrhage is natural. Therefore menstruation is unnatural. He stated, furthermore, that evidence is wanting to prove that menstruation is common in women belonging to the savage races of mankind who live more strictly in accordance with nature, unhampered in their reproductive function by the usages of civilization. The Hindoo women as a rule, he said, do not menstruate. With them menstruation is considered a crime. History, according to King, does not furnish unequivocal evidence that menstruation was common in ancient times, and he quoted the Scriptures in proof of this statement.

Menstruation as a True Secretory Process.— A comparatively recent article by James Oliver (1906) embodies a new conception of the menstrual process. This author believes that menstruation must be looked upon as a definite secretory process on the part of the endometrium. He states, for example, that the menstrual process often makes its appearance while the individual is asleep in the recumbent position. The amount of blood then lost is not materially different from that lost by the same individual when the discharge appears during active locomotion. It is noteworthy, he says, that female acrobats and contortionists engaged actively in their pursuits lose no more than other women. Again, the increase of blood to the generative organs caused by sexual excitation does not disturb the tenor of menstruation unless perhaps this influence is exerted when the function is actually in existence. When the menstrual discharge is retained in cases of imperforate hymen or other obstruction, menstruation still takes place month after month, until perhaps several pints of fluid have accumulated. It is practically impossible to conceive that this could take place purely and simply from capillary rupture, since this is a relatively feeble cause and would be soon annulled. Accumulation of the menstrual blood to this extent, however, is compatible with the theory of secretion, for secretory pressure is a powerful force. Again, worry often causes a menstrual discharge to appear before its time, and mental shock experienced during menstruation may suddenly arrest the flow and hold it in abeyance, not only during the remainder of this period, but for one or two months thereafter. If the denudation theory of menstruation is maintained, these movements of the uterus are inexplicable; if, however, the menstrual fluid is an excretion, then the behavior of the uterus becomes more intelligible. For these and other reasons, Oliver suggests that menstruation should be looked upon as a secretory process on the part of the uterine mucosa.

The Theory of a Menstrual Centre.— The essential features of this theory are as follows: First, the belief that a menstrual centre is situated in the lumbar enlargement of the cord; second, that menstruation is a result of rhythmical changes in this centre; third, that menstruation follows the discharge of vasodilator impulses from the centre, coursing along the uterine nerves to the uterus. Aside from the question of whether or not the pelvic nerves carry vasodilator fibers, we must bear in mind that, as a rule, functional hyperemia is produced by an inhibition of the normal tonic vasoconstriction of the blood vessels concerned. This theory, as usually stated, embodies the idea that the menstrual centre is an automatic one, which in itself is very improbable, inasmuch as all the other centres of which we have knowledge, those of micturition and defecation, for example, are reflex in their nature. Needless to say, the centre governing menstruation has not as yet been definitely located.

Steps Leading to the Modern Conception of Menstruation.— Goltz's experiments (1874), since confirmed by Sherrington and also by Marshall and Jolly (1905), showed that "heat" is not caused by a cerebral reflex.

In one case the spinal cord of a bitch was cut at a point in the lumbar region. Normal pro-estrum, followed by estrus and conception, occurred subsequently, and pups were born after a full time pregnancy. In another experiment of Goltz and Ewald (1896), the lumbar part of the spinal cord was completely removed from a bitch, which afterwards came "in heat" and had pups as in the former case, thus showing that "heat" is not due to a spinal reflex.

The transplantation experiments of Marshall and Jolly, Knauer and Halban, show even more conclusively that the connection between the ovary and uterus is not a nervous one, inasmuch as "heat" reappeared after removal of the ovaries and their transplantation to some other portion of the body. Since all normal nerve connections of the ovary were thereby completely severed, the influence of the latter on the uterus must necessarily have been exerted through the blood stream.

These observations, therefore, bring us to the last big step which has been taken in our rapidly advancing knowledge of menstrual physiology — the step which has been made possible only by the light of the hormone theory. The essential feature of the modern theory of menstruation, as will be shown in the next chapter, is the view that the underlying cause of menstruation is an internal secretion or hormone originating in the ovary.

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CHAPTER VII

THE MODERN THEORY OF MENSTRUATION

The Ovary the Underlying Cause of Menstruation.— Our modern conception of the mechanism of menstruation is based upon the belief that the ovary gives forth an internal secretion, which is responsible for the phenomenon. As we shall see, there are some who take exception to this theory, but the evidence in its favor seems quite overwhelming. The cessation of menstruation after castration, the reappearance of menstruation after successful transplantation of the ovaries, and the occasional appearance of menstruation after administration of ovarian extracts of one form or another, all speak for the essential importance of the ovary in menstruation.

Halban has brought forth evidence, both clinical and experimental, indicating that the ovaries are not quite as essential in the causation of menstruation as we have been accustomed to believe, and that they are rather to be looked upon as activators of the real underlying cause, which probably has its source elsewhere in the ductless gland chain. The interrelation of the various internal secretory structures has long been known, however, and nothing in Halban's work disproves the view that, directly or indirectly, the presence of the ovary is necessary for the occurrence of menstruation.

The Ovarian Influence Exerted through Blood Stream, and not by Nerves.— For many years, since 1832, the occurrence of the menstrual phenomenon has been attributed to the activity of the ovaries. This is exemplified in the theory of Pflüger, which was in such vogue until comparatively recent years, and which explained menstruation as due to a nervous reflex evoked by the ripening of the graafian follicle. In other words, the impulse originating from the ovary was believed to reach the uterus through the medium of nerve channels.

This belief was shown to be incorrect by the striking transplantation experiments of such investigators as Marshall and Jolly, Knauer, Halban and others. These authors demonstrated that menstruation persists even after complete removal of both ovaries — and of course severance of their nerve communications — if they be successfully transplanted to some other portion of the body, perhaps quite distant from their normal site. In other words, the impulse responsible for menstruation must originate in the ovaries, and, just as obviously, must travel by way of the blood stream. It is therefore to be classed among the internal secretions or hormones of the body.

Which Constituent of the Ovary is Concerned with Menstruation? — There has been much discussion as to just which element in the structure of the ovary is concerned in the production of this important hormone. Is it the follicle, the stroma, or the corpus luteum? More and more the evidence is pointing to the corpus luteum as the structure primarily and perhaps exclusively filling this rôle. The father of this theory was Gustav Born, who bequeathed his ideas to his pupil Fraenkel, by whom they were placed upon an experimental basis.

The Corpus Luteum Theory of Fraenkel.— Fraenkel's hypothesis in regard to the underlying cause of menstruation is only a part of his larger theory as to the part played by the corpus luteum throughout the entire reproductive period. He believes, first of all, that the corpus luteum must be looked upon as a ductless gland, which is renewed every four weeks during the sexual life of the human female, and at different periods in the various lower animals. Broadly speaking, it might be said that there is only one corpus luteum, which is regenerated periodically and which occupies different positions in the same or other ovary.

Its function is to maintain the nutrition of the uterus from puberty to the menopause and to prepare its mucosa for the reception and maintenance of the ovum. If the latter be fertilized, the corpus luteum is important in the fixation of the ovum and its nutrition during the early months of the pregnancy. If, on the other hand, the ovum escape fertilization, there is a retrogression of the hyperemia produced by the corpus luteum, which undergoes degeneration until it is, so to speak, renewed in a fresh position. Fraenkel's views were based primarily upon the study of nine operative cases in which the corpus luteum was destroyed by the actual cautery. In eight of these the succeeding menstruation was said to have been missed. A later paper is based upon a much larger material.

Other Modern Views of the Cause of Menstruation.— Theory of Marshall.— Marshall does not accept the findings of Fraenkel. Although he believes that the ovary provides an internal secretion, he considers that this is elaborated by the follicular epithelial cells or the stroma rather than by the corpora lutea. This secretion circulates in the blood and produces a series of changes, which at least assist in the phenomena of heat or of menstruation. After ovulation, which occurs normally in the lower animals during estrus, the corpus luteum is formed, and this organ elaborates a further secretion, the presence of which is essential for the changes taking place during the attachment and development of the embryo in the first stages of pregnancy. Marshall suggests, from these conclusions, that the effect produced by the administration of ovarian extract must vary according to the condition (whether estrous, non-estrous, or pregnant) of the animal from which the extract is obtained.

Theory of Theilhaber.— Theilhaber, also, disagrees with Fraenkel as to the rôle of the corpora lutea in the origin of menstruation. He says that the internal secretion which causes menstruation is produced by the ripening

of the ovum. The farther it is removed from maturation, the less of such secretion does the egg contain, and vice versa. If the unimpregnated egg is thrown off, there is, for a few weeks, a deficiency of this secretion, and the hyperemia of the uterus subsides. As soon, however, as a ripening ovum again produces larger quantities, the amount of blood in the uterus is decidedly increased. This explains the cyclic nature of menstruation. If the ovum is impregnated, it remains in the organism and menstrual hyperemia persists. By the penetration of the spermatozoa into the egg, the formation of the secretions by the egg is greatly stimulated and a greater hyperemia of the generative organs is quickly produced. This is especially true of the uterus, which rapidly increases in size with the increase of the ovum. The ovum itself, so to speak, regulates the condition of the nourishment which it needs. When ovulation is scanty, as in the preclimacteric years, and with cessation of ovulation, as in the postclimacteric years, there occurs gradually a marked stenosis of the vessels of the generative organs with a resulting and permanent anemia. Very little proof is offered by Theilhaber of the truth of this theory that the ovum itself supplies internal secretions which bring about menstruation.

Studies of Aschner.— Another author who does not accept the theory of Fraenkel is Aschner, who states that he has always been able to cause hyperemia and hemorrhage from the genitalia by the injection of ovarian extract, but never by the injection of extract of corpus luteum alone. He also refers to the work of Landsburg and Okintschitz, who reported that corpus luteum extract will often bring about cessation of uterine hemorrhage.

Investigations of Loeb.— Perhaps the most extensive experimental investigations of the subject have been those conducted by Loeb, whose work was carried out principally on guinea pigs. He believes that the uterine cycle in these animals can be divided into two periods. The first, which comprises the changes associated with heat and ovulation, he does not believe is due to the activity of the corpus luteum, but is actually inhibited by it. On the other hand, the second stage, characterized by a decidual reaction and by phenomena of secretion in the uterine glands, depends upon the presence of the corpus luteum. He wisely adds that "menstruation introduces a complication into the cycle, inasmuch as the cessation of growth processes is followed by necrotic changes in the mucosa and by hemorrhages."

Theory of Halban.— Finally, mention may be made of the work of Halban, who also has energetically opposed the findings of Fraenkel. Like other authors, Halban criticizes the methods of study employed by Fraenkel. He himself reports his findings in forty cases in which the corpus luteum had been removed, during the course of operation, for the purpose of studying the effect of the removal upon menstruation. In Halban's cases, the removal was effected by actual excision of the entire corpus luteum, whereas in Fraenkel's cases, as has been stated, an effort was made to destroy the

corpora lutea by means of the cautery point. The latter method, Halban states, does not by any means ensure complete destruction of all lutein tissue.

In 37 of the 40 cases studied by Halban (92.5 per cent), uterine bleeding appeared from two to four days after operation, lasting from three to eight days. Unfortunately, no histological studies of the uterine mucosa from these cases were available to determine whether this hemorrhage was a genuine menstrual flow or merely a single postoperative non-menstrual hemorrhage. It is suggestive, however, that in practically all these cases the following menstrual period appeared four weeks after this postoperative bleeding, which would seem to indicate the menstrual character of the latter. It is of further interest to note, moreover, that the above described phenomenon occurred regardless of whether the operation was performed a short or a long time after the preceding menstrual period. In three cases in which both ovaries were completely removed, uterine hemorrhage occurred two or three days after operation, as in the remainder of the series. Halban explains this as due to the fact that a sufficient amount of the active ovarian substance had made its way into the circulation before the operation to bring on the hemorrhage.

Halban deduces from these observations that the corpus luteum does not cause menstruation, but that the latter is due to ovulation. Like Fraenkel, he believes that ovulation occurs in the intermenstrual period. The corpus luteum, according to him, develops from the ruptured follicle and exerts an inhibitory effect upon menstruation and ovulation both. The menstrual hemorrhage does not occur until the inhibitory influence of the corpus luteum is removed by atrophy of the structure. Ovulation likewise is dependent upon retrogression of the corpus luteum.

Recent Histological Confirmation of Corpus Luteum Theory.— There can be little doubt that the flaws which various observers have picked in the methods of study employed by Fraenkel are in large measure justified. This fact, however, should not prejudice us too strongly against the truth of the theory which he enunciated. It has received very strong confirmation, during the past few years, from a number of investigators whose methods, apparently, leave little room for scientific criticism. I refer to the work which originally emanated from Meyer and Ruge, of Bumm's clinic at Berlin, which has since then received the substantial confirmation of Miller, Schröder and others.

The epoch making contributions of Meyer and others previously mentioned to our knowledge of the life history of the corpus luteum have already been discussed. (Chapter V.) The methods of these investigators were radically different from those of Fraenkel. A large series of cases were utilized by Meyer and Ruge, for example, in an effort to correlate the menstrual history of the patient, the anatomic findings in the endometrium, and the histological stage of development in the corpus luteum. While they differ from Fraenkel as to the exact time at which ovulation occurs, they agree with him that it is in the interval between the menstrual periods.

They also corroborate his finding that a mature corpus luteum is found just before menstruation and they agree that it is the actively functionating corpus luteum that is responsible for the occurrence of the menstrual phenomenon. The life history of the corpus luteum, and its relation to menstruation, as described by these authors, has already been described in a preceding chapter. (Chapter V.) Miller, who has also made an extensive study of this subject, criticizes some of the material utilized by Meyer and Ruge in their investigations, but his own results are substantially in agreement with theirs.

Especially interesting are the studies of Schröder upon the importance of the corpus luteum in menstruation. This investigator asserts that a young proliferating corpus luteum can always be found with the first signs of secretory activity in the endometrium; that a mature corpus luteum is always associated with the premenstrual picture in the endometrium, and that the retrogressing corpus luteum is found with the " status intra- or post-desquamationem mucosae." He states that ovulation occurs at a period corresponding to the fourteenth to the sixteenth days of the menstrual cycle in women who menstruate regularly every four weeks, for it is at this time that the first signs of secretory activity appear in the endometrium. He looks upon the parallel developmental cycles of the corpus luteum and the endometrium as strong evidence that the former is the cause of the menstrual phenomenon.

Injection Experiments.— Up to the present time no definite conclusions are justified by the results of injecting into animals various forms of ovarian extract. Some of the studies, however, have been suggestive. Adler, for example, was able, by injecting ovarian extract, to bring about the characteristic premenstrual swelling of the endometrium. In human beings, also, cases have been recorded in which menstruation was apparently restored by the subcutaneous or intravenous injection of soluble extract of ovarian or corpus luteum extracts. Such observations are, however, too few and too inconstant to possess much significance.

Conclusions as to Cause of Menstruation.— The histological studies above described, added to the clinical studies of Fraenkel and others, speak strongly in favor of the corpus luteum theory of menstruation. The proof, however, can not as yet be considered absolute. For example, it is conceivable that the corpus luteum and endometrial cycles, instead of being related as cause and effect, might both be results of some underlying cause. The problem, after all, is one which must in the final analysis be worked out by the biological chemist.

Were it possible to isolate the active hormone of the corpus luteum, and by injecting it into the blood to bring about the characteristic premenstrual hypertrophic changes in the uterus, the problem would be solved. So far, however, it has not been possible to isolate the active substance of the corpus luteum, and the results of injecting or feeding the various forms of corpus luteum extract, as already mentioned, have not been altogether convincing.

The matter is complicated by the fact that the function of the corpus luteum appears to vary at different stages in its development (Seitz). For the present, therefore, the question must still be looked upon as an open one, although the weight of evidence, it seems to me, is overwhelmingly in favor of the corpus luteum as the ovarian constituent responsible for the menstrual phenomenon.

Influence of Endocrine Glands Other Than Ovary.— Essential as the ovary is to menstruation, it must not be forgotten that the latter function is subject to profound influence by many other endocrine glands. This subject will be discussed in Chapter XXIV. For the present we may merely emphasize that while the entire endocrine system is, in the broadest sense, responsible for the menstrual flow, the ovary exerts by far the most direct influence — it is the portal through which the entire ductless gland chain exerts its effect upon menstruation.

Vascular and Vasomotor Factors in Menstruation.— Assuming, then, that it is the ovary which is primarily responsible for the menstrual process, there are still a number of other links in the menstrual chain which demand explanation. Menstruation is pre-eminently a vascular phenomenon, as indicated by the pelvic hyperemia characterizing it.

How does the ovarian hormone bring about the hyperemia of menstruation? It either acts directly on the blood vessel walls or it produces its effect through the vasomotor nerves. There is some reason for supporting the first of these views, although the second manner of action is more commonly found in the body. Physiologists, I believe, are prone to speak of any relay station in the spinal cord or elsewhere as a "center," and from this point of view some have spoken of a so-called menstrual center, usually described as being located in the lumbar portion of the spinal cord. While there seems to be no definite knowledge concerning such a center, there is no question that the vasomotor nerves of the pelvis play an important rôle — whether essential or only supplementary we cannot say — in the production of the hyperemia which is perhaps the most conspicuous feature of menstruation. The vasomotor nerves are offshoots of the sympathetic nervous system, and through the rami communicantes are linked up with the cerebrospinal system and even with the psychic centers in the brain. These facts are of practical importance in explaining certain types of abnormal uterine hemorrhage.

A Local Factor in the Endometrium.— There is still another factor of importance which must be considered in the explanation of the menstrual mechanism. Hyperemia of the uterine or endometrial blood vessels is not in itself sufficient to explain the exit of blood elements, especially of red blood corpuscles, from the blood vessels toward and into the cavity of the uterus. Such a phenomenon would clash with all our ideas of the usual simplicity of the process of hyperemia. Even in the most intense hyperemia associated with inflammatory processes, there is no such wholesale exodus of red corpuscles from the blood vessel lumina into the surrounding tissues.

No consideration of the physiology of menstruation can therefore be complete without the assumption — though as yet it is little more than an assumption — that a rôle of much importance is played by some local factor in the endometrium which in some way increases the permeability of the blood vessel walls to the blood elements of menstruation. According to Sampson, it is especially the small veins of the endometrium which give passage to these elements. Just what this factor is, how it is formed, and how it acts has not as yet been determined. Much work has been done and is now being done in an effort to solve this problem, but so far the results are very indefinite.

This question is closely bound up with the consideration of why menstrual blood is non-coagulable (Chapter VIII). Whether the same local factor is responsible for the non-coagulability of the menstrual blood as well as for its passage through the vessel walls, and whether the substance is a hormone or an enzyme, are questions which cannot as yet be answered. In the final analysis, however, it seems very probable that the formation of the substance in the endometrium is dependent upon the ovarian function. Perhaps, as Schickele's work indicates, the substance is actually formed by the ovaries and given off in the endometrium.

VII

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CHAPTER VIII

CLINICAL CHARACTERISTICS OF NORMAL MENSTRUATION

Introduction.— Although menstruation is in itself a purely physiological phenomenon, it often gives rise to much discomfort, sometimes amounting to actual disability. It is difficult to draw any sharp line between the mild subjective symptoms experienced by many women at this time and the more severe discomfort which is entitled to the designation of dysmenorrhea. In any consideration of the symptom of pain, the personal factor plays an all important part. The subject is further complicated by the well known fact that normal menstruation may occur even in the presence of the most extensive pathological conditions in the pelvis. In general, it may be said that normal menstruation is not accompanied by actual pain, although there is often a sense of heaviness and discomfort in the pelvis. The group of subjective symptoms associated with the occurrence of menstruation is spoken of as the *menstrual molimina.*

Is Pain a Symptom of Normal Menstruation? — An interesting study has been made by Chisholm of the menstrual process in 100 women who were earning their living by industrial, professional or domestic work. The information on which her paper is based was derived from the women by means of a questionnaire. Since no pelvic examinations were made, the results obtained cannot be safely taken as applicable to the normal woman. This fact no doubt explains why Chisholm found that only 23 per cent of the women were absolutely free from pain or nervous disturbance, and that 77 per cent had some form of pain or discomfort. Even in her series only 3 per cent, however, had pain so severe as to be sometimes incapacitating, although there is little doubt that the series included a certain number of women with pathological alterations of the pelvic organs.

Although 77 per cent of the patients in Chisholm's series had some form of pelvic discomfort, she points out that in 45 per cent it was described as occasional or slight, and a further 12 per cent complained only of irritability, melancholia, headache, and such other nervous symptoms.

Chisholm gives the following table showing the comparative frequency with which pain occurs in girls and in adult women:

PERCENTAGE OF PAIN INCIDENCE

	GIRLS	ADULTS
Free from pain	58.6%	23%
Occasional slight pain	19.2%	18%
Slight pain or discomfort	14.4%	50%
Occasionally or always severe	5.8%	16%
Incapacitating at times	2.0%	3%

A somewhat similar study by Marie Tobler, based on 1020 cases, gave a total of 84 per cent in which some form of menstrual disturbance was experienced. This includes not only those in which pain was complained of, but also those in which other physical or mental symptoms were noted.

Finally, I may mention the results of a study by Dr. Mary A. Hodge of 974 ostensibly healthy girls in the gymnasium classes of the Public Athletic League of Baltimore. For these figures I am indebted to Dr. Wm. A. Burdick, director of the League. Of the 974 girls studied, 660, or 68.8 per cent, suffered no pain at menstruation, while 314, or 31.2 per cent, experienced various degrees of pain. This latter group was subdivided as follows:

(a) Those with "occasional slight pain," numbering 78. Setting aside this group there were left 236, or 24.1 per cent of the total series, with any really significant pain.

(b) Those with "occasional moderate" or "occasional severe" pains, numbering 20. Setting aside this group, again, there were left 216 cases, or 21.1 per cent of the entire series, who may be said to have experienced habitual menstrual pain.

(c) Those with severe pains, requiring rest in bed for one or more days each month, numbering 152, or 5.3 per cent of the total number.

This study would seem to demonstrate the fallacy of the view held by many that more or less pain is the rule with menstruation.

SITE OF PAIN OR DISCOMFORT.—Chisholm gives the principal locations of the menstrual disturbance, especially pain, in girls and adults respectively, in the following table:

LOCATION OF MENSTRUAL PAIN

	GIRLS	ADULTS
Pain in abdomen	35% } 67%	32%
Indefinite discomfort, mostly referred to abdomen	32% }	
Pain in back alone	6.3%	6.4%
Pain in back and front	6.3%	9.6%
Pain in legs	5.5%	19%
Instability or mental disturbance		15%
Headache or general physical disturbance	2.8%	19%

Other Subjective Symptoms of Menstruation.— Other symptoms frequently noted in the menstruating woman are headache, a general sense of lassitude, depression and nervousness, irritability of the bladder, impairment of digestion, sometimes constipation, and occasionally nausea or even vomiting. Not a few women suffer with pain about the breasts, usually slight, but occasionally quite sharp and lancinating.

In some women the thyroid becomes swollen during menstruation, giving rise to increased fullness of the neck. Digestion is sometimes impaired, and often the breath is rather heavy. Krieger found diarrhea in almost one half the cases he studied, although toward the end of the period, constipation was quite frequent. Salivation has been noted, but is not common.

Many women exhibit overactivity of the skin, characterized by increased sweating. The sebaceous glands of the vulva and perineum also become overactive. A similar activity of the sebaceous glands of the face sometimes give rise to acne-like pustules. The occurrence of various other menstrual eruptions will be discussed in Chapter XXV. The face is apt to be rather pale, and in some women "dark rings" form under the eyes. The bladder symptoms consist especially in increased frequency of urination. These would seem to be explainable by the pelvic hyperemia associated with menstruation, in which the bladder also shares to a certain extent.

Statistics of Character and Severity of Subjective Symptoms.— Gebhard, in Veit's *Handbuch der Gynäkologie,* states that a minority of women suffer no discomfort during menstruation, the majority complaining of such symptoms as headache, a feeling of pressure in the abdomen, lassitude, loss of appetite, mental irritability and a tendency to weep. Somewhat similar generalizations are made by Martin, Fehling, and Pozzi.

Jane Ketcham, in 1911, made a study of this subject in 200 women, varying in age from 10 to 45 years, and embracing school girls, college girls, factory girls, clerks, stenographers, and school teachers. Like Chisholm's study, this investigation was based on the responses to a questionnaire. While few figures are given, the statement is made that the large majority of women suffer little or no pain at the onset of menstruation, i. e. during the time the function is becoming established. In 5 per cent of Ketcham's cases the flow was preceded by nausea and vomiting, varying in severity and lasting from one to several hours.

In factory girls, aged 16 to 25 years, there were many cases of acute pain for a few hours, although the great majority complained only of general malaise, often with headache. In the older women, such as the school teachers, aged 25 to 40 years, in the earlier years of their menstrual history they had either had no pain or else it was comparatively slight. As the years had gone on, however, the menses had become increasingly painful, often causing incapacitation from work. The question, "Do you follow your regular work at this time?" brought a rather surprising response. Clerks, stenographers and school teachers often found it necessary to rest

occasionally, while mothers of large families, often engaged in quite laborious work, rarely found it necessary to depart from their usual routine work.

Perhaps the most exhaustive study of this subject, however, is that of Marie Tobler, based on a careful analysis of the menstrual histories of 1020 women. The following table presents in a graphic way the results of her study — the character and intensity of subjective symptoms, as well as the time of appearance of the symptoms:

CHARACTER OF SYMPTOMS	No. of cases	Per cent	TIME OF APPEARANCE OF SYMPTOMS		
			Pre-menstrual Per cent	Intra-menstrual Per cent	Pre- and intra-menstrual Per cent
1. No discomfort	161	15.8	..	..	..
2. Slight local discomfort	45	4.4	..	..	..
3. General symptoms without local discomfort	70	6.9	34	30	36
4. General and local symptoms both	149	14.0	24	39	37
5. Psychic disturbance without local symptoms	80	7.8	57	26	17
6. Psychic and local symptoms both	57	5.6	44	32	24
7. General and psychic symptoms without local sign	117	11.5	27	13	60
8. General, psychic and local symptoms	270	26.5	14	16	70
9. Actual increase of well being	34	3.3	12	67	21
10. Increase of well being, with some discomfort	37	3.6	38	57	5
Total	1020		250	280	270

The "Libido Sexualis" and Menstruation.— The *libido sexualis* is, in the opinion of most authors, somewhat diminished during menstruation. Havelock Ellis, on the other hand, is convinced from his extensive inquiries that, while the aversion to coitus at the menstrual period is real, it is not due to any lessening of sexual desire at that time. Gehrung also states that in healthy young girls amorous sensations are normal during menstruation.

However this may be, there seems to be general agreement among authorities that sexual feeling is heightened just before and just after menstrua-

tion. (Krafft-Ebing, Adler, Kossman, Guyot, etc.) The inquiries of Campbell among a large number of cases, indicate that in two thirds of the entire number in which a connection had been observed between menstruation and the sexual desire, the latter was increased either just before, during, or just after the flow.

It must be said, however, that the existence of a relation between menstruation and sexual desire has been denied by some authors, especially those who are opposed to the view that there is any analogy between menstruation in woman and estrus in the lower animals. The latter period is the period of sexual desire among animals. It has, however, already been emphasized that it is the premenstrual rather than the menstrual epoch in woman which corresponds to the period of heat in the lower animals (Chapter II).

Elizabeth Blackwell, in her work on "The Human Element in Sex," states that the menstrual discharge in itself gives complete relief for the sexual feelings in women, thus comparing them to the nocturnal emissions of men. This opinion of Dr. Blackwell, as Ellis points out, is a survival of a belief which was prevalent a century or more ago, when various writers regarded menstruation as a "device of Providence for safeguarding the virginity of women."

The "Menstrual Wave" Theory.— The menstrual symptoms are by some looked upon as due to the presence in the circulating blood of certain products which reach their maximum just before menstruation begins (Tobler, Schickele). This concept is at the bottom of the so-called "menstrual wave" theory. Although the "menstrual wave" is often alluded to as "Stephenson's wave," the theory had been enunciated by Raciborski in 1868, some fourteen years before the appearance of Stephenson's paper.

In 1878 was published the much referred to work of Mary Jacobi on "The Question of Rest for Women During Menstruation." According to her observations the body temperature of the woman rises from 0.05°C to 0.44°C in the week before menstruation, and falls during the progress of the menstrual bleeding from 0.03°C to 0.25°C, seldom getting quite down to normal during the period.

In the same year with the publication of Jacobi's paper came that of Goodman on "The Cyclical Theory of Menstruation." According to Goodman, the vital activities of women progress in wave-like fashion, the length of the waves corresponding to that of the intermenstrual intervals. Each of these waves exhibits an ebb and a flow, in which there is a decrease and then an increase in such vital factors as the body temperature, the blood pressure, the pulse beat, etc.

Stephenson's paper, "On the Menstrual Wave," was published four years later, in 1882. According to him the maximum of the temperature increase occurs, not at the beginning of menstruation, but about five days before. Otherwise his assumption of the "menstrual wave" differs in no material way from that of Goodman.

The publication of a detailed study of 57 women during 68 menstrual

periods by von Ott in 1889 added a strong confirmation to the theory that the pulse rate, blood pressure, body temperature, and muscle power, all increase before the beginning of menstruation, and then diminish with the onset of the menstrual bleeding. Other writers who have at various times supported this general belief are Chazan (1888 and 1899), Schüle (1896), Gebhard (1898), Schröder (1898), Martin (1899), Fehling (1900), Merletti (1900), Brennecke (1902), Bumm (1902), Marie Tobler (1905), Jung (1907), Siredey and Francillon (1905), and others.

On the other hand, Halliburton (1893), ver Eerecke (1897) and Meyer (1890) have expressed disagreement, largely on the ground that the observations were not carried out exclusively on healthy women. Bayer (1906) also expresses the opinion that the term "menstrual wave" has not, to say the least, been conducive to progress in the study of the phenomenon of menstruation. He emphasizes the advantage of the term "menstrual period."

The best recent study of this problem has been that of Viville (1912). This investigator seems to have avoided the objections which had been made to the work of many of the previous writers on the subject, because he exercised the greatest care in the selection of his 46 patients, and regulated the conditions surrounding the study. His findings, in brief, are as follows: (1) The blood pressure is increased during menstruation in almost the same proportion of cases as it is decreased, and is increased or decreased in about the same proportion of cases during or after the periods. (2) The same statement may be made of the pulse rate and the body temperature. (3) The muscle power in the right or left hand (estimated by the dynamometer) is increased or decreased in about an equal number of cases.

In other words, he finds no evidence to support the view that there are wave-like fluctuations in the activity of these various body functions, corresponding to the menstrual cycles.

A word of detail may now be added with regard to the effect of menstruation upon the various functions which have been already alluded to in the discussion of the "wave theory," i. e., the body temperature, the blood pressure, the pulse rate, and the muscle power.

Effect of Menstruation on Body Temperature.— The first observation to which I can find reference on this subject is by Fricke (1838), who studied the temperature before and during the periods in 24 young women, finding such slight variations that he concluded that menstruation exerts little or no effect on the body temperature. The work of Jacobi and Stephenson has already been alluded to. Kersch (1882) concluded that menstruation evokes a rise of temperature varying from a maximum of 1.0°C down to 0.7°C.

Similar results were reported by Henning (1882). Reinl (1884) and Giles (1896) both found that the temperature is at its low point at about the middle of the intermenstrual period, rising then gradually to its max-

imum a day or two before the beginning of the menstrual bleeding, after which it drops quite suddenly. Somewhat similar results were arrived at by Murchy (1901) and Van der Velde (1904). Reference has already been made to the work of Marie Tobler, who like other observers, described a dropping of the temperature at the menstrual period. King's recent study (1914) tends also to support this view.

The importance of a premenstrual rise of temperature as a diagnostic sign of early tuberculosis was first emphasized by von Riebold (1896), Turban (1899), and later by Sabourin (1903), Leube (1904), Saugman (1904), Kraus (1905) and Osler (1910). (See Chapter XXV.)

The study of Viville, finally, showed that of 47 patients examined, the temperature was unchanged in 44, that it was slightly raised during menstruation in 1, and lowered in 2, while after menstruation it was raised in none and diminished in none. The indication is, therefore, that there is no characteristic effect exerted by menstruation on the body temperature.

Effect of Menstruation on Blood Pressure.— As far back as 1879 Röhrig, on the assumption that menstruation is due to a stimulation of the ovaries, found that by electric stimulation of these organs he could produce an increase in the blood pressure. Von Ott (1889) stated that in 13 of the 14 cases which he studied, the beginning of the menstrual flow was accompanied by a lowering of the blood pressure. Giles (1896) found it highest at the beginning or on the first day or two of the flow, and lowest at the end of the menstrual period. Wiessner (1899) states that during the catamenia the blood pressure drops about 20 mm., reaching its normal again 3 or 4 days after the cessation of the period.

Viville (1912), in his recent work on the subject, finds, in the study of 47 patients, that 34 showed no change, 6 showed an increase and 4 a decrease in blood pressure during menstruation, while after menstruation none exhibited an increase and 3 a decrease. It would be difficult, from these figures, to ascribe to menstruation any important influence on blood pressure. The same conclusion is reached by King (1914).

Effect of Menstruation on Pulse Rate.— As early as 1779, Borden spoke of the pulse during menstruation as "tense, irregular and dicrotic." This was reaffirmed later by Gonot (1810) and Desforges (1813). The first accurate observations on the variations in the pulse rate under menstrual influence were those of Brierre de Boismont (1842). By auscultatory examination of 104 women, he found in 62 a slight acceleration of the pulse during the menstrual period. In 14 women the increase was striking. The remaining 28 women exhibited either no influence on the heart rate or a slight slowing.

Passing over the work of Jacobi, Goodman, and Stephenson, we may allude to the contributions of Zweifel (1899) and Zuntz (1906), both of whom stated that the pulse is slowed during the menstrual period, after having reached its high point in the premenstrual epoch. Viville (1912), in his 47 cases, found that the pulse was virtually unchanged in 34, increased

in 7 and decreased in 4 during menstruation, and increased in none and decreased in 2 after menstruation. He finds no evidence to point to an influence on the part of the menstrual process.

Effect of Menstruation on the Muscle Power.— The general weakness and lassitude so often noted during menstruation has led to efforts to determine accurately any changes in muscular capacity at that time. As in the case of the variations in pulse, blood pressure and temperature, the work of Viville showed that there is no characteristic effect produced by menstruation on muscle power, as tested by means of the Potain dynamometer. The study of 8 cases by Schmotkin confirms Viville's results. The latter in a series of 41 cases, tested by the dynamometer, found no deviation from the normal in 37.

Effect of Menstruation on Knee Jerk.— An interesting study by King of the knee jerk in women at various phases of the monthly cycle showed that "a period of hyperexcitability immediately precedes or accompanies the onset of the menstrual period; that this is followed by a decline in excitability which continues for a few days after the menses have ceased; and that there is then a tendency for it to rise to a slightly higher level than the preceding during the intermenstrual interval."

Periodicity of the Menstrual Flow.— The remarkable regularity with which menstruation recurs throughout the sexual life of the woman is perhaps the most difficult of explanation of all the characteristics of the process. As is well known, there is in many girls a marked tendency toward irregularity for some time after the inauguration of the function. The statistics of Emmett, based upon 2447 cases, showed that in 72.33 per cent, menstruation was regular from the beginning. In 18.92 per cent it became regular after a certain time, and in 8.74 per cent it was never regular. According to Emmett, the average time required for the function to become regular, when it commenced irregularly, was eighteen months after the first appearance. The proportion of sterile married women who were never regular was shown to be somewhat smaller than that of unmarried women.

Osterloh found that menstruation was regular in 68 per cent of a large number of healthy women he studied, always irregular in 21 per cent, and variable in the remaining 11 per cent.

The most elaborate investigation on this subject is that of Sanes, based on 4500 menstrual histories. He finds that 75 per cent of this series of women menstruated regularly, and 25 per cent irregularly.

Even when a patient believes and states that her menstruation occurs quite regularly every twenty-eight days, it is surprising how frequently a careful record of the menstrual dates will disclose slight deviations from this rhythm. This fact was brought out in an investigation by Foster in 1889. Of fifty-six women whom he studied, in only one instance did he note perfect periodicity, the interval in this case being twenty-six days. The number of menstrual periods observed in each woman varied from five to eighteen. There was a difference of 1 day in 1 case, 2 days in 4

cases, 3 days in 3 cases, 4 days in 8 cases, 5 days in 6 cases, 6 days in 4 cases, 9 days in 4 cases, 10 days in 1 case, 11 days in 6 cases, 12 days in 2 cases, 13 days in 2 cases, 16 days in 2 cases, 17 days in 1 case, and 18 days in 1 case. Out of a total of 380 menstrual periods observed, 45 had taken place after an interval of 28 days, 225 after shorter intervals (the shortest being 16 days), and 110 after longer intervals (the longest being 46 days). And yet all the women in the series were healthy and had stated that they were regular in menstruation.

It is not uncommon to hear women say that they menstruate on the same date each month. Such a statement should make one skeptical as to the woman's accuracy, if we bear in mind the difference in the lengths of the solar months. This is certainly a more logical assumption than to explain the occurrence on the ground of psychical autosuggestion on the part of the woman, as has been suggested.

The Interval Between Menstrual Periods.— The duration of the entire menstrual cycle, in by far the largest number of women, is twenty-eight days. A considerable number, however, menstruate regularly at intervals of twenty-one days, and a few every fourteen days. It is thus seen that the interval of days between the periods is most frequently some multiple of seven, a fact to which some significance was attached by the ancients. Since it is true that menstruation usually begins at the second septenary and ceases at about the seventh, it is not surprising that they ascribed to the figure seven a rather mystic rôle in connection with menstruation.

The predominance of the twenty-eight day type of menstruation over other types is evident from a study of the available statistics. In 1000 cases, studied by Kelly, this type made up fully 94.2 per cent of the cases. He gives the following table showing the interval between the menstrual periods in these 1000 cases:

Table Showing Interval Between Menstrual Periods in 1000 Cases

21 days	22	26 days	5
22 "	1	27 "	1
23 "	6	28 "	942
23–25 "	1	29 "	1
24 "	6	30 "	2
24–25 "	2	31 "	1
25 "	9	35 "	1

The statistics of Krieger show that menstruation was of the 28 day type in 70 per cent of his cases, the next most frequent being the 30 day type (13.7 per cent).

Webster, as well as Hart and Barbour, give 71 per cent as the proportion of cases with an interval of 28 days, and 14 per cent with an interval of 30 days.

The exhaustive study of 4500 menstrual histories by Sanes, already referred to, showed that the most common regular type met with was that of twenty-eight days, which constituted 72 per cent. The 30 day type followed next in frequency, but with only 3.8 per cent, and the 21 day type with 3.3 per cent, etc. The most common irregular types were from three to four weeks, then from four to five weeks, two to three weeks, five to six weeks, etc.

Duration of the Menstrual Periods.— Much variation is seen in the duration of the flow in different women. The important fact, from a practical viewpoint, is that within certain rather narrow limits every woman has her own standard, by which she may judge of the advent of abnormality. The average duration given by Emmett, from the study of a large number of cases, is 4.82 days. Among women who have children, the duration was 4.91 days, while among sterile women it was 4.74 days. Among the unmarried the flow was of a shorter duration than for any other class of women.

The average duration of menstruation, as given by Hirst, is 3 to 7 days; by Garrigues, 4 days; Montgomery, 2 to 8 days; Penrose, 2 to 7 days; Gilliam, 4 to 5 days; Keating and Coe, 4 to 5 days; Ashton, 3 to 6 days; Hart and Barbour, 2 to 8 days. The figures given by most of those authors, however, are not based on personal statistical studies. Kelly, on the other hand, has made an investigation of 1000 personal cases from this standpoint. The duration of menstruation in these cases is given in tabular form, as follows:

Table Showing Duration of Menstruation in 1000 Cases

1 day	15	4–6 days	112
1–3 days	15	5 "	136
2 "	36	5–7 "	83
2–4 "	59	6 "	68
3 "	105	6–8 "	37
3–5 "	85	7 "	122
4 "	115	7–8 "	12

Kelly emphasizes the fact that in those cases in which the duration of menstruation was over six days, the amount was described as excessive. In 200 cases in which menstruation lasted more than six days it was described as free in 52, and as excessive in 68. In other words, in 120, or three fifths of the entire number, menstruation was in excess of the normal. He concludes that " a duration of more than six days is so frequently pathologic that it should never be regarded as normal, unless it is clear from other data that the patient's health is fully up to par." From a physiologic point of view, this association of abnormality in duration with abnormality in amount suggests that the same factor is capable of causing

both. Sanes' recent study, finally, gives the most common duration of the menstrual flow as 3 days, then 4 to 5 days, 5 days, 7 days, and 4 days.

AMOUNT OF BLOOD LOST AT MENSTRUATION

Individual Differences.— As regards the amount of blood lost at each menstrual period, even greater individual differences are seen than in the duration of the flow. Every woman is a law unto herself, so that the menstrual bleeding may be considered abnormally free or abnormally scanty only when it is definitely greater or less in amount, as the case may be, than is customary for the woman.

Methods of Estimating Amount.— The indefiniteness of our knowledge concerning the exact, or perhaps better, the average amount of blood lost with the menses is due largely to the obvious difficulties of measuring or even estimating the amounts. The common method of estimating the amount of blood lost by the number of napkins soiled is crude and inaccurate, although it may serve as a guide to any very great increase or decrease in the intensity of the flow. A more scientific method is that of estimating the amount of blood lost by determining first the exact amount of hemoglobin which may be recovered from the soiled protectives worn during the period.

Amount of Menstrual Discharge.— The widest divergence of opinion exists with regard to the amount of blood lost at the menstrual periods. Hippocrates stated that the amount lost by Greek women was 20 ounces. Galen gave the quantity as 18 ounces. For German women von Haller placed the amount at 6, 8, or 12 ounces, while for English women it was put by Smellie and Dobson at 4 ounces, by Pasta at 5 ounces, and by Freind at 10 ounces.

Gorter, for the women of Holland, gives the amount as not over 6 ounces, and Fitzgerald, for Spanish women, as 14 to 15 ounces. Astruc states that French women lose 8 to 10 ounces of blood, while Baudelocque, for the same nationality, gives 3 or 4 ounces. Magendie merely states that the amount lost is often very great and may be as much as several pounds. Linnaeus, in his "Flora Laponica", states that the women of the frozen north, such as the Samoides, lose only a very small amount of blood, and that only in the summer months, while the Greenlanders have scarcely any discharge. These statements agree with those of various Arctic explorers. Hoppe-Seiler believes that the amount of menstrual blood lost is rarely over about 37 cubic centimeters.

While there is the greatest divergence in the estimates of various authors, it is probably not far from correct to say that in the temperate climate the average amount of blood lost at the menstrual periods is from 2 to 6 or 8 ounces, although, as has already been stated, the individual differences are great. The greater portion of the blood is lost during the first half of the period. With most women, it is perhaps the second day on which more is

lost than on any other, while during the first day, before the flow is well established, the amount lost is usually not so great.

Influence of Menstruation on Blood Picture.— While many investigators have concerned themselves with the study of the alterations produced in the blood picture by menstruation, the conclusions arrived at are not as yet as clearly defined as might be wished. The best recent study of the subject is that of Gumprich, who has also given us a thorough resumé of the literature.

Erythrocytes.— The first contributions were those of Hayem and Reinl, who observed an intramenstrual diminution and a postmenstrual increase in the proportion of erythrocytes. Schwinge, Sfameni, Merletti, and Ricca-Barberis arrived at somewhat the same conclusions. Blumenthal placed the decrease in red corpuscles during menstruation as high as one million per cubic millimeter. A similar decrease was recorded by Carnot and Deflandre, who stated that it is not until the tenth or twelfth day after the beginning of menstruation that the blood again shows the normal number of red corpuscles. Krutschenoff also observed counts as low as three million red corpuscles during menstruation.

The objection to all these studies, as Gumprich has pointed out, is the fact that the number of cases on which they are based is much too small to draw general conclusions, especially since, as a rule, the women were studied during one period only.

The study of seventeen women through three menstrual periods, as reported by Anna Pölzl, would seem to promise more reliable results. This author found in eight of her cases that a few days before the onset of menstruation there is a very definite increase of erythrocytes, as much as one or one and a half millions. This is followed by a fall up to the two days before the onset of the bleeding, while a second rise occurs after menstruation. In the remaining nine cases, however, her results are not nearly so definite, and, in some respects they are rather contradictory.

Gumprich finds that the variations of the erythrocytes are usually only a few hundred thousand, rarely over a million, and never so high as stated by Carnot and Deflandre, Krutschenoff and Pölzl. These fluctuations, according to Gumprich, can scarcely be looked upon as directly related with menstruation, inasmuch as the same individual at times shows an increase, at times a decrease during menstruation.

Hemoglobin.— Similar discrepancies are seen in the opinions of different investigators with regard to the menstrual variations in the hemoglobin content of the blood. Hayem, Reinl, Merletti and Ricca-Barberis describe a premenstrual decrease and an intramenstrual increase in the hemoglobin, while Sfameni, Pozzi, and Blumenthal speak of a decrease during menstruation. According to Pölzl there occur only very slight fluctuations in the proportion of hemoglobin. This is also the conclusion of Gumprich, who states that the slight variations noted can scarcely be attributed to any influence on the part of menstruation.

Leukocytes.— The proportion of leukocytes in normal blood is subject to the influence of many factors. As is well known, a physiological leukocytosis is caused by severe exercise, by a hearty meal, by cold baths, etc. It is scarcely necessary, therefore, to emphasize the care with which deductions must be drawn with regard to the influence of menstruation upon the proportion of white blood corpuscles. Hayem found an increase of from one to two thousand during menstruation. Reinert, Moleschott, Schwinge, Birnbaum, Horvath, and others have also described an increase in the number of leukocytes during menstruation. Blumenthal, on the other hand, observed a decrease in four normal cases. Dirks, in the study of sixteen cases during menstruation, found that all showed leukocyte counts above normal.

Gumprich, while agreeing that in general a moderate menstrual leukocytosis does occur, feels that this statement should be qualified. As a rule the leukocytosis is highest on the first day of menstruation, then drops almost as sharply as it had risen. In addition to the menstrual rise, however, he finds that a study of the blood in the intermenstrual periods often discloses similar periods of increase, almost as marked as at menstruation, so that we must qualify our views of the significance of the usual menstrual leukocytosis.

With regard to the differential study of the leukocytes, as influenced by menstruation, there is considerable difference of opinion among investigators. No definite conclusions were arrived at by Birnbaum, Neusser, Carstanyen and Horvath. Ricca-Barberis described an increase in the number of lymphocytes and an irregular fluctuation in the number of eosinophils. Blumenthal found in four normal cases that toward the end of the menstrual bleeding there was a decrease in the neutrophil polynuclears and a corresponding increase in the mononuclears. The eosinophils also increase regularly. Dirks found in nine of his sixteen cases an increase of lymphocytes at menstruation, in two a decrease, and in the remaining five an increase and a decrease at different menstrual periods. With regard to the eosinophils, his results also are indecisive, since in six cases their number was increased, and in the remainder unchanged. In menorrhagia, incidentally, he found usually a relative leukocytosis with a corresponding decrease in the lymphocytes, and often with eosinophilia. In amenorrhea, on the other hand, he found a relative lymphocytosis and a low eosinophil count. Herman found that the lymphocytes increase significantly during menstruation.

Gumprich asserts that the lymphocyte curve shows such marked individual fluctuations in the direction of either increase or decrease, that he does not hold menstruation responsible for any apparent variation in the number of these elements. The same general rule also, according to Gumprich, applies to the eosinophils.

To sum up, therefore, we must conclude that it has not as yet been dem-

onstrated that menstruation gives rise to any characteristic alteration in the blood picture.

The Sugar Content of the Blood.— Kahler has recently shown that just before menstruation there occurs what he terms a menstrual hyperglycemia, the proportion of sugar decreasing again with the onset of the bleeding, and reaching its minimum at the end of the period. The difference between the high and low points in more than half the cases was as much as 0.03 per cent, in one case even 0.04 per cent, in three cases 0.02 per cent, and less than this in the remainder. Bearing in mind that the normal amount of sugar in the blood is only a little over 0.1 per cent, the significance of these alterations is evident. Kahler looks upon the occurrence of this menstrual hyperglycemia as suggestive, in view of the findings of Chvostek that with each menstrual period there occurs an acute hyperemia of the liver, with swelling of the organ (see Chapter XXV).

Objective Phenomena of Menstruation.— The beginning of menstruation is usually preceded by a discharge of mucus which may continue for several days. On the appearance of the blood, in what might be called the secondary stage, the preliminary discharge becomes gradually mixed with blood until it appears to be blood alone. In the third stage the flow disappears in a manner the reverse of its gradual appearance, becoming lighter in color and less in quantity, until at the end it is unstained and reduced merely to the normal secretions of the parts.

The Menstrual Discharge.— In addition to blood, menstrual discharge contains a greater or less amount of mucin, desquamated epithelial cells, bacteria, and granular debris. Owing to the admixture of mucus, it is usually even more viscid than blood from other parts of the body. The characteristic disagreeble odor is partly due to the decomposition of blood elements and partly to the activity of the sebaceous glands of the vulva.

Menstrual blood, according to Krieger, differs from venous blood in its high water content. The serum of the former contains 93.53 per cent of water, while venous blood contains 90.6 per cent water. Krieger quotes the results of careful chemical analysis made of menstrual blood by Simon, Denis, Vogel and Bouchardat, as follows:

	SIMON	DENIS	VOGEL	BOUCHARDAT
Water.	785.00	825.00	839.00	900.80
Solids.	215.00	175.00	161.00	99.20

Analysis of the solids by three of these investigators shows the following:

	SIMON	DENIS	BOUCHARDAT
Fat	2.58	3.90	2.21
Blood corpuscles	120.40	64.40	75.27
Proteins	76.54	48.30	
Extractives	8.60	1.10	0.42
Salts	.....	12.00	5.31
Mucin	.....	45.30	16.97
	208.12	175.00	100.18

Noncoagulability of Menstrual Blood.— By far the most interesting characteristic of menstrual blood is its non-coagulability, i. e., its power of retaining its fluidity for many hours, in contrast to the rapid clotting of blood from other sources. The well known experiment of puncturing the tissues of the cervix during menstruation brings out sharply the difference in this respect between the menstrual blood and that of the body generally. The blood which oozes from the puncture clots readily, while that which comes from the cervical canal remains fluid.

Reasons for Differences of Opinion.— It is not surprising that this property of menstrual blood has given rise to much speculation and not a little scientific investigation. Unfortunately, the results of different investigators are still widely at variance, partly, no doubt, because of the widely different methods which have been employed to determine the coagulation time of blood. Keller enumerates no less than twenty-one different methods which have been utilized by various investigators. He himself emphasizes the advantages of Bürker's method and the improved technic of Wright in the study of this problem. His own work was carried out by the technic described by Bürker.

Importance of the Problem.— It is obvious that the study of this question is of the greatest importance, not only in connection with the mechanism of normal menstruation, but also as applied to the explanation of pathological uterine bleeding. For the present, however, I can do little more than sum up the findings of those who have tried to explain the non-coagulability of normal menstrual blood.

The Rôle of the Alkaline Cervical Mucus.— One of the earliest studies of the subject was that of Birnbaum and Osten. These authors effectively disposed of the time honored belief that the non-coagulability of menstrual blood is due to the admixture of the alkaline cervical mucus. By mixing this mucus experimentally with fibrin producing substances, they were able to show that not only was coagulation not prevented, but that it was actually accelerated. From further experimentation they conclude that menstrual blood remains fluid because of some property of the blood itself. They suggest that operations performed during menstruation are

apt to be attended with more hemorrhage than at other times for this reason: i. e., the absence from the blood of some element essentiaal to clotting. What this is they are unable to say, although they prove that the serum of menstrual blood has the power to inhibit coagulation, and furthermore, that the coagulation time of the body blood is increased.

The Possibility of a Local Factor in the Endometrium.— Cristea and Denk deny the correctness of the last named finding of Birnbaum and Osten, i. e., they maintain there is no change in the coagulation time of the body blood during menstruation. They believe, on the other hand, that the menstrual blood is rendered incapable of clotting by the abstraction from it by the uterine mucosa of the fibrin ferment. Höfnagel, Bode, and Hartmann all agree with Cristea and Denk that there is no appreciable change in the facility with which body blood clots during menstruation.

Schickele's work seems to indicate that extracts made under proper conditions from the uterine tissues possess the power of retarding the coagulation of the blood. When the patient had suffered with abnormal uterine bleeding, extracts of the uterine mucosa showed a striking inhibitory influence on coagulation. This work, in other words, suggests that the noncoagulability of menstrual blood may be due to some local factor in the endometrium. It has not, however, been shown that this inhibitory property of the endometrium is present only at the menstrual period. Moreover, as Bell pointed out, it is difficult to see how uterine tissue, and especially the mucosa, can be obtained without contamination with uterine blood, and of course, at menstruation, with menstrual blood.

The Possible Influence of Changes in Coagulating Time of Body Blood at Time of Menstruation.— It will be seen from the foregoing that the study of the problem of why menstrual blood does not clot is quite intimately bound up with the study of the changes, if any, which occur in the coagulation time of the body blood at the time of menstruation. The latter question has been recently studied by Adler and, even more extensively, by Keller, who concludes that menstruation in normal women, as well as those suffering with various forms of gynecological disease, exerts no influence on the coagulation time of the blood. He further finds that both the menopause and castration are similarly without effect.

The Absence of Fibrin Ferment in Menstrual Blood.—A study of blood from a series of cases of hematocolpos convinced Bell that its noncoagulability was due to the absence of fibrin ferment. In this study, which he later confirmed by experiments with normal menstrual blood, he showed also that neither the alkaline cervical mucus nor the acid vaginal secretion were in any way instrumental in preventing coagulation.

The Formation of Antithrombin by the Endometrium.— Finally, mention may be made of the interesting results obtained by Dienst, who approached the subject from the viewpoint of the normal physiology of blood coagulation. For the latter process two factors are essential — fibrinogen and thrombin or fibrin ferment. The first of these exists preformed

as one of the proteins of blood plasma. The latter, on the other hand, is formed from thrombogen or prothrombin, which also is present in the blood, and thrombokinase, another substance formed from the destruction of blood and tissue cells. For this last transformation the presence of soluble calcium salts in the blood stream is essential.

Dienst further quotes the work of Howell as demonstrating that definite proportions of fibrinogen and thrombin interact to form the fibrin of the clot, and that the thrombin must be present in the proportion of at least one to two hundred and fifteen in order to effect clotting. He shows further that menstrual blood contains the same amount of fibrinogen as other blood, but that it gives rise to far too little thrombin or fibrin ferment to cause clotting. To this fact he ascribes the non-coagulability of menstrual blood. He shows clearly, by testing blood from the median vein, that the low thrombin content of menstrual blood is not shared by the body blood generally.

He concludes that the really responsible factor is the formation of antithrombin by the uterine mucosa, thus counteracting the activity of the fibrin ferment and preventing clotting. He has even attempted to show that the excessive uterine bleeding of such conditions as myomata is due to an excessive formation of antithrombin by the endometrium.

The Biological Rôle of the Endometrium an Important Factor. — Although no very definite conclusion can be drawn from these various investigations, it will be seen that the trend of modern work is to fix upon the endometrium a biological rôle of great importance in the mechanism of normal menstruation, and, among other things, the responsibility for the non-coagulability of normal menstrual blood. Whether this is due to an addition to or a subtraction from the blood of some important element, and what this element is, can not as yet be definitely stated.

VIII

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CHAPTER IX

PUBERTY AND THE ONSET OF MENSTRUATION

General Considerations.— Puberty is one of the critical periods in the life of woman. It marks the transition from girlhood to womanhood, and is characterized by certain anatomical and physiological changes which indicate the awakening of the sexual apparatus to activity. It would seem that in both sexes the reproductive organs, not being essential to life, are the last to take up their characteristic functions. Up to the age of puberty, all the organs of the body show a gradual development — except the generative organs. Their awakening marks the beginning of what is virtually a new existence for the girl. The growth of the organism up to this time seems to be the result of the potential energy — " the primitive impulse " — derived from the blending of the ovum and the spermatozoön. With the awakening of the sex organs, however, it seems that the burden of further growth and development is taken up by them. Not only are they responsible for the appearance of the so-called secondary sexual characteristics, but they also exert a profound influence on the physical and mental growth of the individual.

General Body Changes at Puberty.— At the age of puberty, there occurs a rather sudden and usually striking acceleration in the development of the girl. Up to this period there are only slight differences in the general development of the two sexes, the girl being often just as angular and " boyish " in contour as the boy himself. There is no noteworthy difference between the external form of the male and female bodies, the general outline of the skeleton, or even in the pelvis. With the onset of puberty, however, the figure of the girl begins to take on the characteristic outline of the woman — the hips become more rounded, the breasts fuller and more prominent, while the nipples also become larger. In some cases the hypertrophy of the breasts may become pathologically excessive, constituting the so-called " diffuse virginal hypertrophy " (Bloodgood). As a result of a general deposit of fat, the lines of the entire figure become softer and more rounded. A growth of hair appears on the vulva, mons veneris, and in the axillary spaces. The change of voice, so characteristic of puberty in boys, is usually less marked in girls.

Changes in Reproductive Organs.— In addition to the above, there occur certain well defined anatomic changes in the reproductive organs themselves. The *uterus* becomes larger and also undergoes a characteristic change in shape. While the uterus of the female child is somewhat flat-

tened, that of the young woman shows a fundus with decidedly convex walls. Furthermore, there is a striking change in the proportion existing between the cervix and the fundus. In the young child the cervix makes up something like two thirds of the entire uterus; in the young woman, before childbirth, the fundus has increased to such an extent that it makes up at least one half of the entire uterus; while after childbirth the fundus occupies usually two thirds of the entire organ. The *tubes and ovaries,* which in the young child are undeveloped, also increase in size at the time of puberty.

Important changes take place, also, in the *external genitalia.* The mons veneris become much more prominent, owing to the deposit of adipose tissue, and as already stated, its skin becomes covered with hair. The labia majora, which are very rudimentary in the young child, become much more prominent owing to a deposit of fat, and a hairy growth appears on their external surfaces. As a result of this increase in size of the labia majora, the labia minora become more or less concealed, in contrast to their prominence in the vulva of the young child.

Psychic Changes.— A radical transformation takes place in the psyche of the girl at this period, for now she becomes conscious, for the first time, of the distinction between the sexes. The exact effect of the new impulse in the girl's life varies according to the temperament of the girl, her environment and associates, and other such factors. A certain element of shyness in the presence of the other sex, a tendency to daydreaming, a strain of romanticism — these are among the numerous manifestations often observed.

Physiological Changes.— The physiological changes which occur at the time of puberty are even more striking than the anatomic. Most important among them are the appearance of *menstruation* and *ovulation.* It is sometimes said that the onset of menstruation marks the beginning of puberty; strictly speaking, however, this is not correct, for menstruation is only one of the phenomena which make up this period of transition.

Menstruation Only One of the Manifestations of Puberty.— Table I gives the results of an interesting study in this connection made upon 3279 girls by Dr. Mary A. Hodge, of the Public Athletic League of Baltimore, under the supervision of Dr. William A. Burdick, the head of the League. The criteria of pubescence were considered to be, not the mere appearance of the first menstrual flow, but such changes as the deposit of subcutaneous fat, with the appearance of a waist line, beginning enlargement of the breasts, the appearance of axillary hair, etc.

The prepubescent group, in whom such changes had not yet appeared, embraces girls of various ages, the oldest being 22 years. The adolescent group comprises those in whom menstruation was present.

The following table gives the number of girls of each age examined, the entire series being subdivided into the three groups designated as "prepubescent," "pubescent," and "adolescent," according to the criteria just

mentioned. The percentage figures refer to the proportionate number of girls at each age classifiable under one or other of the three types. For example, all of the 23 girls of 6½ years, or 100 per cent, were prepubescent. On the other hand, there was 1 girl of 17½ (1.1 per cent) who was also classified as prepubescent.

TABLE I

AGE	PREPUBESCENT		PUBESCENT		ADOLESCENT		AGE
	No.	Per cent	No.	Per cent	No.	Per cent	
5	1	100.					5
5½	1	100.					5½
6	14	100.					6
6½	23	100.					6½
7	33	100.					7
7½	46	100.					7½
8	60	100.					8
8½	64	100.					8½
9	79	100.					9
9½	108	99.0	1	1.0			9½
10	112	100.	0	0.			10
10½	127	96.2	4	3.0	1	0.7	10½
11	114	92.6	9	7.3	0	0.	11
11½	103	78.6	25	19.0	3	2.2	11½
12	90	66.1	39	28.6	7	5.1	12
12½	88	57.5	45	29.4	20	13.0	12½
13	61	37.8	61	37.8	39	24.2	13
13½	38	23.7	49	30.6	73	45.6	13½
14	24	13.4	51	28.7	103	57.8	14
14½	7	4.7	29	19.7	111	75.5	14½
15	4	2.7	22	15.1	119	82.0	15
15½	2	1.3	11	7.1	141	91.4	15½
16	2	1.4	6	4.2	133	94.3	16
16½	0	0.0	4	3.0	126	96.9	16½
17	1	1.1			98	97.9	17
17½	1	1.1			87	98.8	17½
17½+	1 (22 yr)	0.1			658	99.7	17½+
	1204		356		1719	To. 3279	

Age at Which Menstruation Appears.— The age at which menstruation first appears is subject to much variation. It is, furthermore, supposedly influenced by climate, race, and other factors. The most complete statistics regarding the age of the onset which have been compiled in this country are those of Dr. George J. Engelmann. This observer studied over 10,000 cases, from this standpoint, in American born women alone.

He found, first of all, that the *American born* woman is more precocious with regard to the onset of menstruation than the women of other countries in the same zone. His statistics showed that the average age of onset in the United States and Canada is 13.9 years, while in the corresponding temperate zone of Europe, it is 15.5 years. Again, he found that the native American girl is more precocious than the American born girl of foreign parents, although the latter, even in the first generation, closely approximates the American girl of American parents. Racial characteristics, he finds, fade away very rapidly. While the age of puberty in Germany is 15.5 to 16 years, and in Ireland 15.3 years, in the girl born in America of German or Irish parentage it is only 14.5 years. Only the Canadians and French seem to be exceptions to this general rule, for while they begin to menstruate at 14 and 15 in their native land, when born in this country they are more precocious than the Americans of the same class, 13.7 years being the average age. Climate, therefore, seems to have no influence, and race very little. The statistics of Currier, obtained from a much smaller series of cases, give the average of the first menstruation in this country as 14.5 years. Among these, those of American parentage show an average of 14.1, *Irish* 14.75, *Italian* 15.6, *German* 15.6, *French* 12.6, *English* 14, *Swedish* 16.25, *Austrian* 15.6, *Canadian* 14, *Scotch* 16, *Danish* 17, *Russian* 19, *Swiss* 19, *Polish* 16, and *Greek* 13. In *Bohemia* the age of menstruation is between 15 and 16, according to Necos (quoted by Lenz).

The age of onset of menstruation among *Indians* has been studied by A. B. Holder. According to this author, it is not easy to learn the age of puberty among Indians, inasmuch as it is a custom in most tribes for the girls to marry before the menses appear. It might be believed that the early age, and consequent sexual stimulation, together with the entire absence of modesty in action, thought, and conversation, would tend to cause precocious menstruation, and the statistics of Holder seem to confirm this impression. Even in the girls who are in school until after puberty, menstruation seems to appear earlier than in white girls in the same latitude. The cases upon which Holder's report is based were observed in an agency school, under his own personal supervision. The average of this limited number of cases is 12.91 years, and is in accord with the opinion of the other physicians in charge of the Indians on the government reservations.

The question of the beginning of menstruation in the *Japanese* and *Chinese* has been studied by M. Yamasaki. There are five distinct races inhabiting Japan — the Japanese, the Ainos, the Koreans, the Chinese, and the natives of the country in Formosa. There were 4861 Japanese women studied by Yamasaki. The average age of the beginning of menstruation was found to be 14.8 years. The earliest menstruation occurred at 9 years and 7 months; the latest at 21 years and 10 months. From the collected observations of 14 authors, upon 26,082 Japanese women, the average age was 15.05 years. The Chinese women observed were all residents of Formosa, who had emigrated from China long previously. There were 135 cases,

the earliest menstruation being 11 years, and the average 17 years. It will thus be seen that, although the climate of Formosa is warmer than that of Japan, the first menstruation occurred later than in Japan. Of the Korean women there were 184, and the average age of onset was 17 years. Here the beginning of puberty was even later than among the Japanese, although the climate is warmer than that in which the Japanese races live, and colder than that of Formosa. Among the Ainos, 84 women were examined. The average here was 15 years. On the whole, therefore, it will be seen that this extensive study led to a conclusion the opposite of that generally held with reference to the influence of climate. The general opinion seems to be that race and manner of life have a greater influence on the beginning of puberty than climate. Four races here show very little difference, although their mode of life varies greatly. For example, the Chinese women live entirely in the house, while the Ainos hunt and work in the field.

The menstrual history of *Egyptian* girls was studied in 275 cases by Elgood, the girls all attending a boarding school for natives in Cairo and being between the ages of 6 and 16. No child began to menstruate before 12, only 8 at this age, and in the majority the onset occurred at 13 or after. Some did not menstruate until the age of 16 or even later. The examination of the girls in three of the boarding schools in Egypt showed that of 295 girls, between 6 and 11 years of age, not one had menstruated; of 143, between the ages of 12 and 18, 81 had menstruated and 62 had not.

In the study of 624 cases from the arctic zone, mostly *arctic Indians* and *Esquimaux,* Engelmann found the average age of the onset of menstruation to be 14.6 years. In 2733 cases from the subtropical region of *south Asia* (18° and 23° N. lat.), Robertson found the average to be 12.9 years. However, in the tropical zones themselves, where we might expect the age of onset to be very low, the study of 1593 cases of Campbell, Robertson, and others, has shown the average age to be 15.8 years. These cases were collected from Siam (13° N. lat.), Cochin China (11° and 17° N. lat.), Barbados and Demerara (6° and 13° N. lat.), Batavia (8° S. lat.), Somaliland (0° and 10°), and Bogasland (0° and 10°).

Factors Influencing Age of Onset of Menstruation.— To sum up these various statistics, therefore, it will be noted that it is not easy to draw deductions concerning the influence of race and climate. It seems to be true, however, that, contrary to the general impression, climate does not exert a powerful influence upon the age of onset. It has usually been believed that menstruation appears at a much earlier age in warm countries than in cold, but as has been seen, this is certainly not an invariable rule. The influence of race also seems to be less important than generally believed, and the same thing applies to the manner of life.

Individual factors are probably much more important in influencing the age of onset than such general factors as we have considered. The mentality of the girl, her surroundings, her education, her temperament, etc., all stand out prominently as factors which determine precocity in the appear-

ance of the menses. Astruc, one of the old authors on the subject, mentions "Among the things which sooner bring the menses are fever, coition, drinking much, violent emotion, vomiting, sneezing, anger, the hysterical passion, the suppression of a customary evacuation, and emmenagogues. Those things by which the menses are retarded are immoderate cold, sorrow, a sudden fright, too great evacuation, incrassating diet, acridity of humours, acids, and astringent medicines." The importance of some of these factors, it will be seen, is based upon the old "plethora theory" of the causation of menstruation, which Astruc held, in common with most of the authors of his time. In addition to the above, it may be stated that overnutrition, excessive meat diet, and intense mental activity are among the factors which tend to accelerate the menstrual onset. On the other hand, simple, regular and moderate diet, and avoidance of excessive nerve strain or mental work are retarding factors.

Cause of Puberty.— The fact that at the time of puberty there is a rather sudden acceleration of development of the generative organs, and at the same time a striking change in parts of the body not directly connected with the generative tract — the so-called *secondary sexual characteristics* — is the basis for the view which many have supported that these sex stigmata are the direct cause of the awakening of the reproductive organs to activity. According to Roberts (quoted by Biedl) there are primitive people in Russia and in India who attribute these various sexual distinctions to the external genitalia, and, in the case of women, to the breasts. The Russian Skopzi, according to this author, believe that women are rendered sterile by removal of the breasts and external genital organs. The old dictum, "Propter uterum solum mulier est quod est," or, in its revised form, "Propter ovarium solum mulier est quod est," represents the same theory to which Virchow later gave expression in these words: "Woman is woman by reason of her generative glands. All the peculiarities of her body and mind, everything, in fact, which in the true woman we admire and revere as womanly, is dependent upon the ovary." By the secondary sexual characteristics John Hunter indicated all those distinctive sex manifestations which are not directly concerned with the processes of reproduction, including under this grouping such changes as appear in the mammary glands, the skeletal growth, the distribution of adipose tissue, the size of the larynx, etc.

There are some investigators, notably Tandler and Gross, who believe that the secondary sexual characteristics are nothing more than characteristics of the species, and that they have no direct relationship with the organs of generation. As evidence in support of this theory, the fact is brought forth that even in fetuses and new born infants, long before the awakening of the sexual glands themselves, a number of characteristic differences between the sexes are already apparent. For instance, there are differences in the size of the hands and feet, the body weight, the size and weight of the brain, and the bony structure of the pelvis. It has been pointed out, however, that this evidence is far from conclusive, inasmuch as at this early

age, the primary sex glands — the ovary and the testis — are already well differentiated, and it is impossible to exclude their influence in the production of the changes above mentioned. On the other hand, there is much evidence, such as that derived from a study of the effects of prepubertal castration, to justify the generally accepted theory that the changes of which we are speaking are dependent upon the presence of the genital gland, and that they are correctly spoken of as " secondary sexual characteristics."

Essential as the ovary is for a full development of the secondary sexual characteristics, it must not be assumed that it is the only structure which exerts an influence in the production of the various changes included under that head. As we shall see in a later chapter (Chapter XXIV), there is a most intimate correlation of function between the ovary and certain other ductless glands, the most important of which are the thyroid, the thymus, the suprarenal, the pituitary and the pineal body. All of these structures have a possible auxiliary influence in the production of the secondary sexual characteristics. It is probably correct to say that when the correlation of function of these various organs with internal secretions (i. e., the ovary, thyroid, thymus, suprarenal, pituitary and pineal) is a harmonious one, the anatomic and physiologic changes so characteristic of puberty appear in a normal manner. When, on the other hand, there is a break somewhere in the functional chain represented by these organs, there is apt to be some sort of abnormality of puberty, either in its character or in the time of its onset.

IX

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CHAPTER X

THE HYGIENE OF PUBERTY

The Rôle of the Mother.— It would certainly seem necessary to emphasize the very great importance of a proper supervision and régime at this critical period in the life of the girl. As she unfolds into womanhood she is susceptible to all of the many influences, big and little, of her environment and association. To mould her into a healthy type of woman it is essential that these various influences be of a beneficent character. Especially important is it that the atmosphere of the home be of the proper sort. There can be no question that it is the mother, especially, who exerts the most profound and permanent influence upon the character and temperament of the growing girl, and that it is she, especially, who can be of the greatest service to her daughter at this trying period in the latter's life. The truth of this is well exemplified in the many unfortunate cases in which young girls are left motherless. There is nothing more beautiful than the mutual love and confidence of mother and daughter in the ideal home. Happy is the girl with a mother to whom she can go for counsel in the many perplexities which are apt to arise during this transitional period of her life! The girl approaching this period should be prepared by her mother for the advent of the menstrual process, which otherwise might frighten and distress her. Inasmuch as mothers and daughters differ so much in the character of the relationships which they bear to one another, it is obvious that this enlightenment of the girl will be conveyed in various ways, if at all.

Instruction in Sex Hygiene.— No one can quite take the place of the mother in instructing her daughter in the simple and beautiful truths of the reproductive life and its various manifestations. When, however, such home instruction is out of the question, as a result of ignorance or other incapacity on the part of the parent, there is a legitimate field for the activity of various agencies now interested in "sex education" of young people. That such instruction should come only from those who are peculiarly fitted for it, and who at the same time are sane enough to appreciate that there may be an element of risk mixed with it, goes almost without saying. It is the conviction of the writer that, especially in the case of girls, such talks do far more good when given to the girls individually rather than in large groups, as is so often the case. He also feels that in addition to giving "sex hygiene" talks to young girls directly, much good can often be accomplished by instructing the mothers regarding the advisability of enlighten-

ing their own daughters. There is scarcely anything in which human beings differ so much as in their attitude toward the big problem of sex, and hence the cardinal note in sex instruction should be individualization — the adaptation of the matter and method of instruction to the individual case. Such delicate instruction should not be handed out indiscriminately.

School Life.— Next to the influence of the home itself, the most potent factor in moulding the character and health of the girl at the time of puberty is, in the majority of cases, the influence of school life. There can be no question that the tendency of recent years has been to crowd too much into the curriculum of the school child. This seems to be especially true of the public school systems of most of the large cities of the country, although even the private schools are not blameless in this respect. This is still true, notwithstanding the great advances made in this respect in recent years by many educational institutions, for the physical betterment of their pupil bodies. It would seem as if the acquirement of much knowledge, often in the nature of mere "book learning," has been the sole ambition of modern life. Laudable as such an ambition may be, it may be pushed to such a limit as to be unnatural and unwise. These terms are justified when we consider that the educational wave has left in its train thousands of young girls — we are discussing more especially the "feminine" aspect of the problem — who are broken in health, neurasthenic, and anemic.

Such serious inroads upon the health of the young girl, coming just at this crucial period, leave a lasting impression upon her body, mind, and soul, and many an invalid woman is the end product of the delicate, overworked schoolgirl. The more ambitious and conscientious the girl, the greater her application to her studies, and the greater the liability to injurious effects upon her health. What has been said in this connection applies especially to the unreasonably great amount of home work which is assigned to girls in many schools. After spending many hours in class rooms, pupils are obliged to devote a great many more to these home studies, leaving very little time for the conscientious student to devote to purposes of recreation. And all this at a time of life when the girl is especially in need of relaxation, and when lack of it is most apt to leave a lasting impress upon her.

Working Conditions.— In the class of girls who are obliged to work for a living at a very early age, equally injurious effects upon the general health may be produced by occupations which deprive the girl of adequate rest and recreation. This evil is in a measure mitigated by the fact that many states now have laws regulating the age at which a child may be sent to work, and also the maximum number of hours during which she may work. In spite of this fact, however, there are still thousands of girls who are compelled to perform work distinctly injurious to them at or about the age of puberty, when they are most in need of fresh air and recreation. Long hours of standing in department stores, or sitting at a table making cigars, or sewing in poorly lighted and ill ventilated tailoring shops — any

one of these, as well as a long array of other similar occupations, lay the foundation of future ill health and perhaps invalidism in thousands of cases. In the individual case it is the duty of the physician to point out the dangers of such occupations as these to young girls, and, in so far as it may be possible, to give counsel as to an amelioration of the injurious conditions. On the other hand, it is equally the duty of communities to make such things impossible by the enactment and enforcement of wise laws governing the employment of children.

Recreation and Rest.— Just what form of recreation or exercise is best suited for the girl in this growing stage will of course depend in great measure upon the individual case. Exercise in the open air is unquestionably a necessity for the fullest health at this period of life. Walking, though not so popular as formerly, is one of the very best forms of outdoor exercise, and should be encouraged among young girls. Any of the numerous games so popular among boys and girls are also of value in this respect, for, in addition to the purely physical advantage of the outdoor exercise, the spirit of the game increases the recreational advantages. The same statement applies to any of the ordinary forms of outdoor sport — tennis, rowing, swimming, croquet, riding, etc. Needless to say, even these may be abused when carried to an immoderate degree. Calisthenics and gymnastics may be indulged in, either indoors or in the open air, although the latter is, of course, the preferable way.

Dancing has always been a popular form of diversion among young girls, and there is no doubt that the graceful stepping and balancing which it entails are of distinct physical advantage. On the other hand, it can not be denied that distinct harm results from dancing when practiced in the intemperate manner so frequently seen. The exhilaration of the dance has a great tendency to make the dancer forget her fatigue, and like overexercise of other kinds, the harm of such dancing more than counterbalances any good that may come of it. From a purely moral standpoint, of course, there are serious objections to many of the dance halls seen in most of our large cities, and it is gratifying to know that many of our municipalities have already taken steps toward the establishment of municipal dance halls, conducted along proper lines. This advance is especially important from the standpoint of the working girl, whose long hours of monotonous work make her eager to find some rather exciting and perhaps violent form of pleasure and diversion, often at the expense of the sleep which is so essential to her health. From eight to ten hours sleep should be obtained by the average girl in the growing period of life.

Clothing.— With regard to what might be called personal hygiene, it need only be said that this is largely a matter of common sense. Unfortunately, in some matters common sense is antagonised by Dame Fashion, and, with perhaps the majority of young girls, the latter is apt to come off victorious. In this connection, the incongruities of the feminine apparel of the present day at once suggest themselves. The fashion of the narrow skirt

has unfortunately returned, for a time at least. Aside from its inconvenience to the wearer it is iniquitous from a hygienic standpoint, for it is incompatible with naturalness of gait, and tends to produce an incorrect attitude of body. Society still demands that the dictates of common sense be set aside in dressing for receptions, balls, the theater, and other such places of amusement, and that decolleté gowns, thin stockings, and light slippers be worn instead of those of heavier and warmer character. It is not surprising, therefore, that such functions are frequently followed by colds, sore throats, and perhaps even worse sequelae, often seriously undermining the health of the girl.

The same may be said of the rather prevalent fad among girls of wearing as little underclothing as possible, and of wearing the same light summer undergarments all the year round. This is done with the idea of "toughening" themselves, so to speak, and thus rendering themselves less vulnerable to colds. While there are, no doubt, many girls who may do this successfully, the frequent and oftimes great changes in our climate make it risky for perhaps the majority of girls. For these, it is no doubt safer to don heavier underclothing with the advent of the cold weather, and to change the upper apparel accordingly. While no general rule can be laid down for all girls, it may be said that the body should be sufficiently warmly clad to prevent any chilling of the surface.

Bathing.— It is scarcely necessary to more than mention the importance of personal cleanliness. Aside from its cleansing function, the daily bath produces a feeling of exhilaration and well being which is in itself a sufficient reward for taking it. The bath should preferably be taken in the morning, though as a matter of convenience many take it later in the day. If the bath be not taken every day, certainly it is more or less essential to bathe at least twice a week, especially in warmer weather. A strong, robust girl will enjoy a daily cold bath, but perhaps the majority of girls, especially those who are at all delicate or anemic, prefer it more or less warm, especially in cold weather. The bathroom should always be comfortably warm, and the bath should be followed by brisk rubbing with a rough towel, so as to provoke a healthy reaction. Cold baths should not, generally speaking, be taken during the menstrual period, or just before the flow is expected, for fear of bringing about a suppression of the function. Even at this time, however, a warm bath may be taken with comparative impunity, although most girls and women rely upon a daily sponge bath instead. Here again the personal equation comes into play. For example, there are some girls who take a cold plunge every morning, and who suffer no ill effects even when this is kept up during the menstrual periods.

Diet.— The frequency of digestive disturbances among young women makes it advisable to call attention to the faulty habits of diet so commonly seen among them. The strong, healthy girl is just as apt to have a good appetite as her strong, healthy brother. When it is poor and capricious, therefore, it is frequently due to the fact that instead of making her meals

of plain, substantial food, the girl has been indulging too strongly in "dainties", such as candies and pastries of various sorts. In other cases — and these are becoming increasingly numerous — the poor appetite or the stomach disturbance is due to excessive drinking of coffee or tea, the use of both having been increased to such an extent that they are now looked upon as necessities of life. If used by the growing girl at all, it should be only sparingly. The drinking of milk and considerable quantities of water is much more beneficial.

Care of the Bowels.— Attention should be called also to the importance of a proper care of the bowels, for the constipation so often seen in young girls, and which so often persists throughout subsequent life, is in not a few cases due to carelessness and neglect. Both in the case of schoolgirls and of working girls defecation is often postponed for one reason or another, until finally a habitual constipation is the result. This is a matter of considerable importance, and girls should be strongly advised to heed the calls of nature with as little delay as possible. In this way it may be possible to avoid a condition of chronic constipation which is apt to be more or less intractable once it has developed.

Other Hygienic Measures of Importance.— As at other periods of life, the proper care of the eyes, the ears, the nose, the throat, and the teeth is of the greatest importance. It is necessary merely to allude here to these hygienic measures, for their detailed consideration is scarcely within the scope of such a work as this. The importance of such measures of personal hygiene to the developing girl can, however, scarcely be overestimated. The habits of life formed by the girl at this susceptible and flexible period of life are likely to persist in later years, and hence may exert a vital influence upon the entire course of her physical life.

X

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CHAPTER XI

PRECOCIOUS MENSTRUATION

What Constitutes Precocious Menstruation? — Although the average age at which menstruation begins in this country is about 13.9 years, there are many cases in which the age of onset is considerably lower than this. As a matter of fact, menstruation may occur in very young children, and even in newly born infants. Unless the variation from the usual age of onset is very great, the case may be looked upon as representing merely an individual but not pathological peculiarity. If the variation is extreme, however, as in the case of newborn infants, the case must be considered one of pathologically precocious menstruation. It is difficult to fix an arbitrary dividing line between normal and precocious menstruation, inasmuch as there are many individual factors to be considered. Speaking generally, however, it may be said that if menstruation begins and recurs regularly in a girl of less than 9 years of age, in this climate, it must be looked upon as precocious. Lenz sets the age before which menstruation is to be considered precocious as 8. A considerable proportion of girls commence to menstruate between the ages of 8 or 9 and 14. These cases may be looked upon merely as cases of unusually early menstruation. According to some recent German statistics, menstruation occurs between the ages of 8 and 12 in 3.5 per cent of all cases (Mayer and Kriger), 2.9 per cent (Schlicting), 5.7 per cent (Schaffer), 2.7 per cent (Grusdeff).

Early Manifestations of Premature Development.— The history of these cases of precocious menstruation shows that some evidence of precocious maturity is very often observed at the birth of the child. In some cases it is the unusually large size of the child, in others the prominence of the breasts, or the presence of hair on the vulva.

In view of the fact that body growth ceases a comparatively short time after puberty, the precocious onset of the latter would seem to be capable of exerting a marked influence on the extent of the skeletal growth, by bringing about early ossification of the epiphyseal cartilages. This has been emphasized by Tandler. Cushing, in referring to the studies of the latter, says "that the normal individual in whom adolescence occurs at an early age remains, as a rule, short limbed, whereas those with a tardy adolescence are long limbed. In other words, early sexual development indicates early closure of the epiphysis; delayed puberty (of which artificial eunuchism represents the extreme example) suggests delayed epiphyseal union."

Frequency.— As to the frequency of precocious menstruation, it is

difficult to arrive at any accurate opinion, because of the fact that many cases are not reported. Owing to the increasing interest in the study of the physiology and pathology of menstruation, many more are now finding their way into the literature than in former years. Up to 1800 only 18 cases had been recorded. By 1900 the number had increased to 107. The most complete recent report on the subject is that of Lenz, who has studied the records of 130 cases which have been reported from 1680 up to 1913. Since then a number of additional cases have been reported by Gengenbach, Beekman, and others, sending the total up to one hundred and fifty-one cases.

Age at Which Precocious Menstruation May Be Observed.— As to the time at which the onset of menstruation is noted in these cases, there is a wide variation, as may be seen from the subjoined table of Lenz. In the 130 cases which he collected, menstruation was observed as follows:

At the time of birth	in	1 case
Immediately after birth	"	2 cases
2 days after birth	"	1 case
14 days after birth	"	1 "
15 " " "	"	1 "
2 months " "	"	1 "
3 " " "	"	3 cases
4 " " "	"	4 "
5 " " "	"	2 "
6 " " "	"	3 "
7 " " "	"	3 "
8 " " "	"	1 case
9 " " "	"	9 cases
10 " " "	"	2 "
1 year	"	9 "
1¼ years	"	1 case
1½ "	"	11 cases
1⅓ "	"	1 case
2 "	"	10 cases
2¼ "	"	1 case
2½ "	"	1 "
2¾ "	"	1 "
3 "	"	14 cases
3¼ "	"	1 case
3½ "	"	2 cases
4 "	"	13 "
5 "	"	6 "
5¾ "	"	1 case
6 "	"	5 cases
6½ "	"	2 "
7 "	"	2 "
Exact time unknown	"	14 "
Total		130 cases

Lenz calls attention to the curious fact that the beginning of menstruation occurs most frequently at some period which is a multiple of 9 months. For example, at the age of 9 months 9 cases occurred; at the age of 1½ years (2 x 9 months), 11 cases; 3 years (4 x 9 months), 14 cases; 6 years (8 x 9 months), 5 cases. He believes that if the age at which the flow appeared in these cases had been more accurately studied, it would be seen that this interesting rule would be even more apparent. In view of the fact that 9 months is the length of pregnancy in women, and that menstruation is ordinarily absent during pregnancy, he suggests that the above observation points to a congenital origin of the tendency to precocious menstruation.

Types of Precocious Menstruation.— According to Lenz, there are three types of precocious menstruation. In one group of cases the premature onset of menstruation is accompanied by maturation of the sexual organs, and is associated with the evidences of general bodily development which ordinarily characterize puberty — the rounding of the figure, the growth of pubic and axillary hair, etc. This group embraces the majority of cases of precocious menstruation. In the second variety of the phenomenon, the precocious menstruation and the development of the reproductive organs again are observed, but in connection with tumors involving the suprarenal, pituitary body, or other ductless glands. In the third group, seen only in a small minority of instances, the precocious menstruation occurs in the entire absence of any other manifestation of premature activity on the part of the generative organs.

As will be gathered from what has been said, precocious menstruation is only one, though perhaps the most important, of the symptoms of precocious development of the entire reproductive apparatus, and this in turn is usually only one manifestation of precocious development of the body generally. As contrasted with precocious menstruation (*menstruatio praecox*), some authors speak also of *pubertas praecox* and *evolutio praecox*. It may be well to distinguish between these three terms. By "menstruatio praecox" is meant the discharge of blood at regular periods from the generative tract of girls below the age of nine. "Pubertas praecox" is the term employed to indicate the complex of anatomical and physiological changes in the external and internal generative organs of girls below the age of nine, characterized by certain changes in the breasts, the distribution of hair, etc., together with the appearance of certain periodic processes of which menstruation is the most important. Finally, by "evolutio praecox corporis," Lenz has reference to the array of symptoms associated with an accelerated development of the reproductive system, together with a premature stimulation of bodily growth. The latter shows itself in an increase in the size as well as weight of the body, an accelerated growth of the entire skeleton, and a premature ossification of the epiphyseal cartilages — all these symptoms occurring in girls below the age of nine.

Clinical Manifestations.— The two most common symptoms of pre-

mature development in female children are precocious menstruation and mammary hypertrophy, often with the appearance of milk in the breasts (Fig. 25). We have already spoken of the age at which precocious menstruation may appear. The amount of blood lost at the menstrual periods in these cases is ordinarily not very large, to judge from the cases in which mention is made of this feature. In Morand's case the flow lasted always for three days. In Wetzler's case the duration was five or six days, Le Beau's three days, Susewind's two days, Loriot's three days, etc. In other words, the duration of the menstrual flow in these cases seems to vary from two to five or six days, much like the variations in the duration of menstruation in normal women.

In a few of the cases which occurred in somewhat older girls, the patients complained of symptoms similar to those experienced by adult women at the time of menstruation. Thus in the case of Caesarano, that of a girl of seven who had commenced to menstruate at the age of six months, there was a complaint of backache with each menstrual period. In Korsakov's case, while the age of the girl is not given, it is remarked that she frequently suffered with hysterical convulsions at the menstrual periods. A similar hysterical tendency was noted in the case recently reported by Lenz. Again, in the case of Plyette, that of a girl of four, mention is made of the fact that the patient suffered with a vicarious flow from the nose.

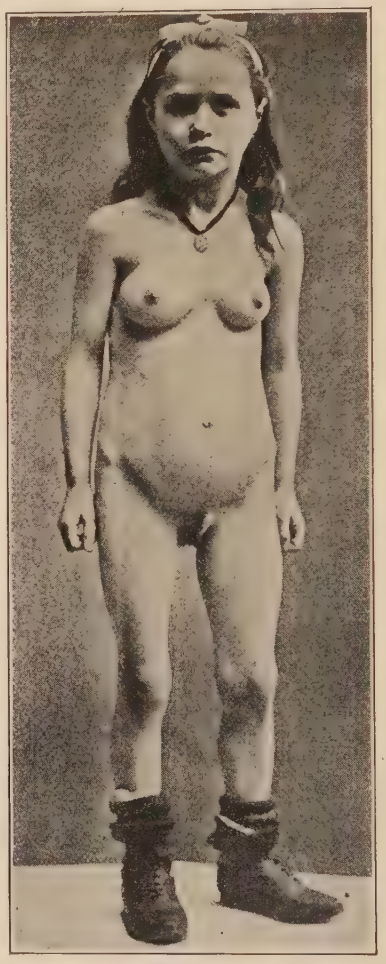

Fig. 25.— Precocious Development in a Girl of Six.

The size and general appearance are those of a child of at least thirteen years. Menstruation had been regular since the age of six months, the periods lasting 3 or 4 days. Note the development of the breasts (Lenz).

Subsequent History of Patients with Precocious Menstruation.— It must not be assumed that in all of these cases menstruation continues uninterruptedly up to the time of the menopause. Such a course, as a matter of fact, seems to be the exception rather than the rule. In some cases menstruation is irregular throughout, as in those of Cooke, Korsakov, and Lenz. In other cases it is regular for a time and then ceases altogether. In Klein's case the periods occurred regularly for four months, were followed by a period of amenor-

rhea, and ceased altogether following an attack of measles. In the case of Tulpius menstruation was regular from the age of four to the age of eight, when it ceased, being followed by severe attacks of headache. On the other hand, in some cases menstruation has commenced at a very early period, and has continued without interruption — except when due to pregnancy or lactation — for many years. Perhaps the most notable example of this is the well known case of Anna Mummenthaler, reported by von Haller in 1751. This patient menstruated regularly from the age of two. At nine she became pregnant and gave birth to a child. Menstruation continued regularly up to the age of fifty-two, the woman reaching the age of seventy-five.

Psychic Development.— In spite of the physical precocity in these cases, psychical development is as a rule very poor. In the case reported by Lenz the child still played with dolls and small children at the age of ten. Practically all authors speak of the childish type of mind in these cases. In one case only, that of Bouchut, is there an exception to this rule, the author speaking of the character as being "earnest" or "serious." Reference has already been made to the case of Korsakov, in which hysterical convulsions occurred at the time of the menstrual epochs. Onanism is mentioned in the reports of three cases, those of Kornfeld and Nacke, and that of Olinto, the latter case being characterized also by "nervous alterations." Lenz speaks of the legend that the child Mohamed had as his concubine the eight year old Kadisha, although Velpeau believes that this is based upon an incorrect translation of the Koran.

Pregnancy in Cases of Precocious Menstruation.— To show the extent to which sexual maturation may advance at very early ages, it is interesting to note that quite a number of cases of pregnancy have been recorded in girls who exhibited precocious menstruation. Perhaps the most remarkable of these is the case reported by Mandeslo, of a child who commenced to menstruate at the age of three, and who gave birth to a son at the age of six. In addition to this case Lenz has collected 10 other instances of childbirth at ages ranging from eight to twelve years, reported by von Haller, Sue, d'Outrepont, Ramon de la Sagra, Montgomery, Rowlett, Carus, Smith, Molitor and Bodd.

Cause of Precocious Menstruation.— In the majority of cases, no definite anatomical explanation can be found for the occurrence of precocious menstruation or of precocity in the other manifestations of puberty. In view of our ignorance concerning the exact cause of normal puberty, we can only say that premature puberty, like the normal process, is probably due to a stimulus arising in some way from the ductless gland chain, and especially, of course, from the generative glands.

Much weight is given to this theory by the autopsy findings in a number of reported cases. Guthrie and Emery, and also Hofacker, have reported cases in which tumors of the generative glands have been found at autopsy in cases of precocious puberty.

Even more conclusive are several cases in which such tumors have been removed at operation, with disappearance of the signs of early puberty. In the case of Lucas the signs of prematurity, especially the prominent mammae, disappeared after the removal of a sarcoma of the ovary. Brohl records the case of a girl of seven, with precocious menstruation and the development of a mature woman. A large cystic ovary was removed, and, although kept under observation for two years after the operation, she did not menstruate again. A similar case, occurring in a child of nine years, has been reported by Sacchi. The most recent case reported is that of Harris, whose patient was five years of age. The precocious menstruation in this case, as well as other manifestations of premature development, disappeared completely after the removal of a carcinomatous ovarian teratoma of the right ovary. Numerous cases have also been recorded in which tumors of other ductless glands, notably the suprarenal, pituitary, pineal and thyroid, have been associated with symptoms of sexual precocity. Bulloch and Sequeira, as well as other authors, have described such cases. The tumors most frequently found in these cases are hypernephromata.

Neuman, in 1901, reported 22 cases of precocious maturity associated with tumors of the pineal gland. Very few autopsies are recorded in cases of precocious menstruation in which there was no tumor present, either in the ovaries or in the other internal secretory glands. Indeed, I have been able to find reference to only one, that of Prochownik. This patient began to menstruate at the age of one year, flowing every four weeks for two or three days, up to her death, from bronchitis, at the age of three. At autopsy there was found but little development of the breasts, which, however, contained gland tissue. Hair was present in the axillae and about the external genitalia, which were well developed. The uterus, both from the standpoint of its size and of the proportion between the cervix and body, was far beyond the normal for the age of three. The endometrium presented the appearance usually seen in the adult uterus after menstruation, while the ovaries gave indication of regular ovulation.

Diagnosis of Precocious Menstruation.— This is easy, except perhaps in those cases which develop within the first few days after birth. During this period it may be difficult to distinguish the condition at once from the simple non-menstrual hemorrhage of the new born (see Chapter XII).

The two conditions may be distinguished by the fact that non-menstrual genital hemorrhage usually occurs at about the fifth or sixth day after birth, while menstruation does not as a rule appear until later; that genital hemorrhage occurs only once, while menstruation recurs with greater or less regularity; and that genital hemorrhage is not associated with the other signs of premature development which are so frequently present with precocious menstruation.

The only other condition, from which it is necessary to differentiate precocious menstruation, is that associated with the precipitation of urates

from the urine of infants, often giving rise to the presence of a brick red deposit on the diapers. On casual examination this might be mistaken for blood. If there is any doubt concerning the real character of such stains, it may very easily be cleared up by microscopic examination.

Mention should also be made of the value of the X-ray, both for diagnostic and purely scientific purposes. It gives the best evidence of somatic development by depicting the advanced stage of skeletal development in these cases of precocious maturity. This has been emphasized by Lenz, Neurath and Wolf. The bones are larger than normal for the age, and ossification is farther advanced than would be expected; the epiphyses often being fully joined to the shafts, or else being separated by only thin discs of cartilage. Special attention is called to the pelves of such children, for in many cases they resemble those of the fully matured woman.

Treatment of Precocious Menstruation.— Medicinal treatment is never required in these cases. The time will probably come when organotherapy will be of prime value in the treatment of this, as well as other menstrual disturbances. At present, however, our knowledge of this subject is so imperfect that no intelligent plan along these lines can be suggested.

As Morse emphasizes, the psychological treatment of these cases of premature development is of much importance. The frequent early development of sexual desire, long before the development of will power, exposes these children to the danger of violation, as is shown by the many cases of very early pregnancy which are recorded. Every effort should therefore be made, along individual lines, to prevent them from such unfortunate accidents.

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CHAPTER XII

NON-MENSTRUAL GENITAL HEMORRHAGE IN THE NEW BORN

Differentiation from Precocious Menstruation.— It is probable that many cases which have been reported in the literature, particularly the earlier literature, as cases of precocious menstruation were in reality instances of hemorrhage of non-menstrual character. It has been known for many years that hemorrhage not infrequently occurs from the genitals of new born female infants within a few days of their birth. The differences between such hemorrhages and those indicative of early appearance of the menstrual function have already been mentioned (see chapter on "Precocious Menstruation"). Briefly, the main points of differentiation are the appearance of non-menstrual bleeding usually within the first week of life, its failure to recur as in menstruation, and the absence of other secondary sexual manifestations. It is true that, in exceptional cases, non-menstrual genital hemorrhages have recurred once or even several times, as in Kerkring's patient, quoted by Halban. Such an occurrence, however, is exceedingly rare.

Frequency.— Among 10,000 new born female infants Shukowsky found 35 cases of genital bleeding; a proportion of 1 to every 285. Bilhard, by an actual study of the uteri from 700 new born girls, found evidences of uterine bleeding in only two cases. Lequeux and Marioton put the proportion of such cases at 0.61 per cent, Renouf at 2.59 per cent, Zacharias at 2.5 per cent, and von Winckel at 0.12 per cent. Halban, from a histological study of 21 cases, claimed to have determined the existence of genital bleeding in eight, giving the rather startling proportion of 38.09 per cent. In a similar study of 12 cases Zacharias found bleeding in 1, or 8.3 per cent. Single cases have been reported by a number of American authors. From these figures, it may be gathered that while genital hemorrhage in the new born is, comparatively speaking, a rare occurrence, the frequency of its recognition would be no doubt much increased were a careful histological study made of the vaginal secretion in all of a given series of cases.

Time of Occurrence of Bleeding.— In the majority of cases, the bleeding is noted on about the sixth or seventh day. Shukowsky, in his large series of cases, had never observed it before the fifth day. On the other hand, Purefoy, Engström and Frew have observed it even on the first day of life, Bride and Carus on the second, von Winckel on the third, and Pollak and Cullingworth on the fourth. Bednar and Ritter found it to be

most common on the fifth day. Zacharias, in 10 cases, observed the bleeding on the fourth day in 3, on the sixth in 4, and on the seventh in the remaining 3. It will thus be seen that, while genital hemorrhage may occur on any one of the first seven days of life, it is much more frequent on the sixth and seventh days than on the first five.

Duration of Bleeding.— It is exceptional for the bleeding to continue longer than a day or two. In 6 of Zacharias' cases, it continued 1 day, in three 2 days, and in one 3 days. Jardine, however, speaks of a case in which the bleeding lasted 4 days, while Busey mentions one in which it continued 4½ days, Pollak one of 5 days' duration, Bates one lasting 7 days, and Engström one in which the bleeding was present for 8 days. Such long durations as these, however, are quite exceptional.

Amount and Character of Bleeding.— The bleeding in these cases is practically never severe, and usually, as a matter of fact, is drop-like in character. Often it is so slight as scarcely to be noticeable, although Busey and Jardine have reported cases in which the hemorrhage was quite profuse. According to Gebhard, as much as 30 gms. of blood has been lost with this type of bleeding.

In many cases the bleeding is introduced by an increased secretion of mucus. The clear appearance of the latter then gives way to a bloody discoloration, until often a drop of blood, or perhaps a blood clot is noticed on or between the labia. In other cases there seems to be no preliminary mucous discharge. The blood is bright red in color, later becoming dark brown or even chocolate colored. Microscopically, according to Jardine, the blood presents no pathological alterations.

Accompanying Symptoms.— Many authors attribute significance to various clinical symptoms not infrequently associated with the bleeding. For example, Shukowsky believes that all infants who exhibit this phenomenon suffer from intestinal disturbances. Others lay stress on a septic factor, while Eross observed in such cases an acute catarrh of the mucosa covering the pars vaginalis. Frew, in his case, noted that convulsions were associated with the bleeding. On the other hand, most authors, including Zacharias, Juda and Engström, speak of the entire absence of any associated symptoms.

Prognosis.— Opinion is virtually unanimous among writers that the prognosis in such cases is favorable. Only Busey is inclined to believe that it is not unassociated with danger to weak children.

Etiology.— Although many hypotheses as to the cause of genital hemorrhage in the new born have been suggested by writers on this subject, none has gained general approval and acceptance. It is of interest to review a few of the explanations which have been offered for the phenomenon. Shukowsky, finding intestinal disturbances frequently associated, attributed an etiological rôle to them. He suggested that, by inducing a general visceral hyperemia, they predisposed to such hemorrhages. Von Winckel gave hemophilia as a causative factor in one of his cases, the mother being a

sufferer from the disease. Ritter looks upon the bleeding as the manifestation of an existing sepsis. Dolóris believes that some infection of unknown nature caused the epidemic-like appearance of genital bleeding in five infants in an obstetrical ward at the same time, four of them dying. Hennig believed that congenital cardiac insufficiency causes some cases of this type, the bleeding being only an indication of the associated passive congestion. Asphyxia of the new born babe has also been held responsible. According to Henoch, papillomata of the vulva or vagina may cause bleeding; as may also sarcoma of the ovary (Gautier). The possibility that genital bleeding may be caused by trauma either during or after delivery, cannot be gainsaid. Zacharias lays stress on the fact that it is in large babies especially that such hemorrhages are seen. He quotes von Winckel, and also Lequeux and Marioton, as emphasizing this fact, and finds in his own series of 10 cases, that the infants weighed from 3150 gm. to 4840 gm., as compared with the average of 3000 gm.

The theory of Halban alone is based upon a scientific study of the question. By a careful macroscopic and microscopic study of 8 uteri from which more or less hemorrhage was taking place, he established the fact that the local process was quite similar to that found in normal menstruation, thus confirming the earlier observation of Zappert. According to Halban, the capillaries of the mucosa were always filled with blood, as well as the submucous and periuterine vessels. Here and there hemorrhages were seen extending under the epithelium. Defects of the latter were not seen, except occasionally a flattening due to the pressure of the escaping blood.

Halban also demonstrated that the ovaries in such cases gave no evidence of active function, and he therefore sought elsewhere for a possible cause of the menstrual picture in the uterus. This he attributed to the presence in the fetál circulation of substances formed in the maternal placenta, which thus acts as an organ of internal secretion. The placental secretion produces a hypertrophy of the fetal uterus, so that, as a matter of fact, the organ is larger at the time of birth than it is for some time afterward. Halban essays to prove these statements by the dimensions of the uterus at birth and afterward, as given by various authors. He himself found the average length of the uterus in 11 new born infants to be 3.2 cm., while the average for infants who died at ages varying from three weeks to two years was 2.5 cm. In addition to the increase in the size of the uterus, Halban states that the placental secretion brings about a hyperemia of the uterus which may reach a grade sufficient to cause active bleeding after delivery. The recent experiments of Schickele, Aschner, and Fellner seem to substantiate Halban's view in that extracts of placenta when injected into the circulation are stated to cause an increase in size of that organ, with vasodilation and a tendency toward hemorrhage.

Treatment.— In view of the slight amount and the short duration of the bleeding in practically all cases, no treatment is necessary. Various measures have been recommended, apparently " ut aliquid fiat." Thus,

Busey gave in his 2 cases small doses of the fluid extract of hydrastis canadensis. Juda, again, has made use of a 10 per cent gelatin solution in dram doses several times a day. Biedert advises that warm baths be not given during the bleeding. It is doubtful, however, whether any of these measures have any effect on the bleeding, which tends to cease spontaneously.

XII

LITERATURE

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CHAPTER XIII

THE MENOPAUSE

Definition.— The menopause marks the termination of the reproductive stage of a woman's life, the most prominent clinical manifestation of this transition period being the cessation of the menstrual flow. The menopause is also often spoken of as the climacterium or climacteric, while among the laity it is most frequently called the "change of life."

Historical.— Although menstruation itself was the subject of much speculation among the ancients, as we have already seen (Chapter I), much less attention seems to have been given to the phenomenon of the cessation of the menstrual function. By the old school of humoral pathologists, the cessation of menstruation was looked upon as a matter of serious consequence, often causing serious disorders and calling for the operation of blood letting. Perhaps these old observers are in part responsible for the great dread with which the menopause is even now looked forward to by a large proportion of womankind.

Currier quotes Hoffman, one of these humoral pathologists, as saying that, "if venesection is omitted when the menses cease, violent cardialgias will result, accompanied with intense heat and pain about the precordia, the back, and scapulae, especially in the night time. Others will suffer with intolerable heat, pain in the joints, and erysipelatous fevers, while still others will be affected with nephritic disorders accompanied with pain in the loins, and terminating in calculous concretions. Furthermore, some women, after their sixtieth year, have discharges of bloody urine, or are seized with immoderate discharge of their menses, which at last terminates in an hectic. Some women, especially those who are wasted by prolonged grief, have been afflicted with pain in the left hypochondrium accompanied with uneasiness and heat in the precordia, which afterwards terminates in a violent vomiting of the blood or the morbus niger of Hippocrates. In such patients, upon opening their bodies, the spleen has been found preternaturally large and putrid, the vasa brevia of the stomach ruptured and gaping, and the blood discharging from these vessels into the ileum." In this description it is not difficult to recognize the "intolerable heat" as the distressing vasomotor flushing and the flashes of heat from which the climacteric woman is so wont to suffer, while the "immoderate discharge of their menses which at last terminates in an hectic" clearly has reference to the cancerous disease which is so apt to occur at this period.

In the same connection, Hippocrates states: "We learn from experience

that exulcerations, violent and even scirrhous tumors of the uterus, are sometimes produced by cessation of the menses. Neither do the external parts of the body escape the fatal consequences of such suppression, since we know from experience that by this means they are frequently affected with the itch, the elephantiasis, boils, erysipelatous disorders, or scirrhous tumors." Here again, we have an unmistakable, though crude, picture of cancerous disease. The middle ages brought very little new knowledge concerning the nature of the climacterium, and, as was said concerning the study of menstruation in general, it is during the past fifteen or twenty years that most of our new knowledge concerning this subject has been contributed.

The Age at Which the Menopause Occurs.— As with puberty, the age at which the menopause occurs is subject to wide variation. As a general rule, in this climate, menstruation ceases between the ages of 40 and 50, and in my experience, more frequently between the ages of 45 and 50 than between 40 and 45. In a series of 100 white women in Baltimore, representing various nationalities, I found that 58 ceased to menstruate between 45 and 50, 30 between the ages of 40 and 45, 3 below the age of 40, and 9 above the age of 50. The extremes noted in this series were 27 years and 54 years. The most recent statistical study of this question is by Sanes, who collected the literature from thirty-two nations. He finds the average menopause age of all the cases to be 47.1 years. This figure is somewhat higher than those of Currier, who in a series of 96 women, found that 30 stopped menstruating between the ages of 45 and 50, 31 between the ages of 40 and 45, 27 below the age of 40 and 8 above the age of 50. The extremes were 30 and 53 years. The statistics of Kisch, based on the study of 500 German women, correspond closely to my own. In 455 cases he found that the menopause occurred in 48 between the ages of 35 and 40, in 141 between the ages of 40 and 45, in 177 between the ages of 45 and 50, and in 89 between the ages of 50 and 55. In Berlin, Mayer studied 1546 cases, giving an average of 47.04 years. Among French statistics may be mentioned those of Leudet, who found the average age of the menopause for women in easy circumstances to be 47.4 years; for those obliged to work hard for a living 48.7 years; and for those who lived in the country 47.9 years.

The histories of 1082 English and French women, analyzed by Tilt, showed the average age of the menopause to be 45.7 years. According to Börner, the average for the women of northern Europe is higher than that for the women of southern Europe. Other statistics, quoted by Currier, are those of Rodsewitch, who gave the average for St. Petersburg women as 48.7 years; Binsenger, who at Moscow found it to be between 40 and 43; and Hanover, who found the average age of 312 cases studied in Denmark to be 44.82 years.

Finally, from an investigation conducted by Currier upon the menstrual function in native American women, it appears that in the Sac and Fox

tribes, menstruation ceases at about the age of 48; in the Crow and Assiniboine at 49 or 50; in the Uintah, between 40 and 50; in the Apache, between 42 and 53, while in the Cheyenne and Arapahoe the extremes were 46 and 73, and in the Sioux 38 and 58 years.

From a study of these various reports, it would appear that Webster is correct when he says, concerning the age at which the menopause occurs, that " in temperate countries it takes place in about fifty per cent of women between forty-five and fifty; in twenty-five per cent, between forty and forty-five; in twelve and one-half per cent, between thirty-five and forty; and in twelve and one-half per cent, fifty and fifty-five." From what has been said as to the age of onset of the menstrual function (Chapter IX) it will be seen that the average duration of the menstrual life of woman is about 32 years.

Factors Influencing the Age of the Menopause.— Speaking generally, it seems to be true that the earlier the menstrual function is established the longer it will continue. In other words, if puberty occurs at an early age, the menopause is apt to be late in its appearance, the reverse being true also. This is contrary to the view commonly held by the laity. Gallant has worked out a table of " approximate ages " at which the menopause should normally occur, the age at which menstruation first appeared being known. These figures refer to women who are free from any form of disease, pelvic or otherwise. The table is as follows:

Year in which menses appeared	*Year in which menopause should occur*
10th	50th and 52nd
11th	48th and 50th
12th	46th and 48th
13th	44th and 46th
14th	42nd and 44th
15th	40th and 42nd
16th	38th and 40th
17th	36th and 38th
18th	34th and 36th
19th	32nd and 34th
20th	30th and 32nd

If menstruation continues very long after the expected age the possibility of some pathological condition being present should be borne in mind.

Maternity.— According to Sanes the climacterium is usually late in the case of women who have led an active sexual life, especially if they have given birth to a number of children. On the other hand, it is apt to occur early in unmarried women.

Climate.— It is stated that the climacteric occurs earlier in the women of cold climates than those of the tropics. Inasmuch as menstruation is said to make its appearance earlier in hot countries than in cold, this fact, if it be a fact, can be explained only on the assumption that the duration of the entire reproductive period is shorter in cold than in warm climates.

Race.— Although statistics bearing on this point are meager and rather contradictory, it seems to be true that certain races and nationalities exhibit an earlier average age of menopause than others. To illustrate, the Arab women of the desert are cited as examples of those showing a characteristically early menopause, this not infrequently being observed between the ages of 20 and 30.

Heredity.— An unusually early or an unusually late menopause is said to be noted in certain families as a hereditary trait. Examples of such families are cited by Currier and others.

Social Condition.— The menopause, as a general rule, occurs earlier in poor, hard working women than those living in idleness or in luxurious surroundings.

Obesity.— It has long been known that the menopause is frequently seen at a very early age in stout women, although the explanation for this fact is comparatively recent. Cases of this type are now looked upon as due to a deficiency of the pituitary secretion, producing the "adiposogenital dystrophy" of Fröhlich. The two most prominent symptoms of the latter are obesity and sexual hypoplasia, manifesting itself in the women as scanty menstruation or an actual cessation of the process. This subject is treated more fully in Chapter XVIII. In these cases menstruation often ceases at an unusually early age. I have seen the menopause occur as early as the age of 23 in cases of this type.

Wasting Diseases.— General diseases associated with wasting and general debility tend to bring about an earlier menopause than usual, the cessation of the function in such cases being apparently an effort on the part of nature to conserve the strength of the woman.

Pelvic Disease.— In the great majority of cases the effect of local disease in the pelvis is to delay the occurrence of the menopause. Among pelvic conditions capable of producing this effect are cancer, other uterine neoplasms, polypoid endometritis, adnexal inflammations, ovarian neoplasms, etc. Rarely pelvic disease may bring about the early disappearance of menstruation. This is illustrated by a case of my own — that of a woman of 34, in whom the disappearance of the menstrual flow was brought about by the presence of bilateral dermoid cysts of the ovaries, destroying practically all ovarian substance.

Early Menopause.— Many cases are recorded in the literature of unusually early menopause. Kisch, for example, speaks of a Hungarian Jewess, fat from childhood, who menstruated at the age of 9, married at the age of 15, was sterile, and ceased menstruating at the age of 17. In another case of the same type, he states that menstruation occurred at 13, marriage at 16, and the menopause at 20. Mayer reports 2 cases in Berlin in which menstruation ceased at 22. One of these is interesting in that three children were born after the menopause. In 2 other cases of Mayer menopause occurred at 25. One of these menstruated once in her twenty-fifth year, after her second labor; she subsequently, after a severe fright,

became idiotic. In still another of Mayer's cases the menopause occurred at the age of 29 in a very stout woman who had previously borne six children. I have already spoken of the case of my own, in which menstruation ceased at the age of 23 in a woman who had borne three children. I have records of a number of other less pronounced cases, in some of which obesity was present and in some of which it was absent.

Delayed Menopause.— In probably more than 10 per cent of all cases menstruation does not cease until after the fiftieth year of life, but it is uncommon for it to continue beyond the age of 55. I have seen one case in which the menopause did not occur until after the age of 57, but many in which it took place beyond the age of 50. Numerous more or less remarkable cases of delayed menopause are to be found in the literature. Currier has collected quite a number. One of the most remarkable of these is the case reported by Battey of a woman 93 years old who still menstruated regularly. Another of equal or greater interest is that of Pitou, whose patient menstruated six months during her seventy-second year, then became pregnant, and aborted at the second month, the fetus being recovered. Sumpter reports 4 cases of regular menstruation in women of 60, 70, 77 and 80 years. Royle speaks of 2 cases in which the climacteric occurred at 67 and 93, and Norton of one in which it was observed at 67. Finally, Neuman has collected a number of reports of cases from various sources, in which the menopause occurred at ages ranging from 60 to 104. In spite of these reports, the fact remains that it is rare for menstruation to continue as late as the sixtieth year, and cases of this kind which are reported should be subjected to close scrutiny as to the authenticity of the age and the genuineness of the menstrual flow.

The Surgical Menopause.— It has long been a guiding principle in gynecologic surgery to avoid complete removal of ovarian tissue in young women for fear of bringing on an artificial menopause, with its train of untoward symptoms. The usual teaching has been that the surgical menopause thus produced is usually sharper and more severe than the normal climacterium. There is much evidence, chiefly clinical, against the correctness of this view. It is a well known fact, as Culbertson states, that the effect of castration on young women is often surprisingly slight. Of the correctness of this statement I am convinced, as a result of many personal observations. Culbertson remarks that not one of a considerable series of young women in whom both ovaries had been removed suffered sufficiently to induce her to continue treatment.

Others who have emphasized the relative mildness of the artificial as compared with the natural menopause are Graves, Pfister, and Fehling. Graves believes that the so-called menopausal vasomotor symptoms are observed with practically the same frequency after removal of the uterus, either with or without removal of the ovaries, as after total ablation of ovarian tissue alone. He ascribes the causation of these symptoms not to mere withdrawal of the ovarian hormone, but to a "break in the utero-

ovarian functional harmony". He therefore considers that there is no advantage in conserving ovarian tissue when hysterectomy is necessary, and that such retention may be actually harmful.

The practical importance of this question is great. It is probable that most surgeons, appreciating the internal secretory function of the ovary, will still continue to practice conservation of healthy ovarian tissue whenever possible. On the other hand, important as the ovary is, it is by no means essential to life or to the maintenance of good health, and ultra-conservatism may sometimes work more harm to the patient than so-called radicalism. The course to be followed in the individual case must be influenced by many other factors than the mere consideration of the physiological function of the ovary. Most important among these factors are the importance to the patient of future childbirths, the character and extent of the pelvic lesions, the patient's age and her economic and social status. For a fuller discussion of this subject the reader is referred to the papers of Culbertson, Graves, Schickele, Polak, and others.

Duration of Menopause.— There are marked individual variations in the duration of the menopausal period. It must be borne in mind that the cessation of the menstrual function is only one, though perhaps the most striking, of a whole group of changes which mark the retrogression of the reproductive function. Properly speaking, the menopause embraces all these various phenomena, and from this viewpoint, its duration is from a few months to several years. Occasionally cases are seen in which the onset of the menopause is very abrupt and its duration brief. Much more frequently, however, its course is more gradual, and its duration therefore considerably longer. The average duration may be placed at from two to two and a half years.

Symptoms of the Menopause.— General Course.— Before describing the various symptoms of the menopause in detail, it may be well to sketch briefly the course it pursues in what may be considered a fairly typical case. As the woman approaches the climacteric age, even while the menstrual function is still regular, she is apt to experience more or less of the vasomotor disturbance which, next to the disappearance of the menses, is the most important manifestation of the menopause. From time to time there will be an intense though transitory flushing of the head and neck, accompanied by a sensation of flashing heat. This is frequently followed by sweating, sometimes copious. The temperament of the woman is quite likely to undergo some change, though only exceptionally is this very profound. Usually this change is evidenced only by unusual nervousness, irritability, and peevishness. By this time there has probably been more or less disturbance of the menstrual rhythm. Whereas the menses have been recurring at regular four week intervals, and have been lasting perhaps four or five days, they now become usually more scanty, lasting only a day or two, and there may be a complete skipping of one period. This may be followed by scanty menstruation for a month or two, and then will come

another period of amenorrhea. In this gradual manner the menstrual function tapers off into complete disappearance. The vasomotor symptoms usually continue for a longer or shorter time after the cessation of menstruation, their disappearance also being gradual as a rule. In the majority of cases there is a tendency to laying on of adipose tissue, sometimes amounting to an actual obesity.

This description will apply to the case of moderate severity. With some women, however, the symptoms are so slight as to be practically negligible. With the exception of the cessation of the menses and perhaps an occasional slight flush, no other symptoms may be observed. In other cases, on the other hand, the menopause may bring about the most violent upheaval in the woman's mental and physical make-up. The vasomotor disturbances may be exceedingly annoying, while the psychic changes may be most distressing, amounting in rare cases to an actual insanity of one type or another, when there is a hereditary tendency in this direction. We shall now consider, in greater detail, some of the important symptoms of the menopause.

Cessation of Menstruation.— Whatever other symptoms a woman may exhibit at this period, certainly the one which gives the menopause its name — the cessation of menses — is the most characteristic. As already emphasized, it is only one manifestation of a retrogressive change involving the entire reproductive apparatus, just as the initiation of the menstrual function at puberty is only one of the signs of the awakening of the sexual life which marks that period. Occasionally the menstrual function may stop very suddenly, but such cases are unusual. Far more frequently, the cessation of menstruation is gradual, as described above, many months frequently elapsing before the "dodging period" gives way to a complete and permanent disappearance of the flow.

It will be noticed that no mention has been made of excessive hemorrhage as a symptom of the menopause. As a matter of fact, the dictum has been laid down that "menorrhagia and metrorrhagia are never caused by the menopause," to quote one author. In my opinion, this statement is true only when properly qualified. There is no question that not infrequently uterine hemorrhage occurs at the time of the menopause in the entire absence of any demonstrable anatomical change in the uterus or other pelvic organs, as will be shown in Chapter XXII. Such cases of "climacteric hemorrhage" are explained as being due to a physiological lesion rather than an anatomical one. The disturbance in these cases undoubtedly involves some portion of the ductless gland chain, being obviously due to the withdrawal of the ovarian secretion. There is thus produced a disturbance of the hormone equilibrium, which sometimes results in bleeding. The condition is analogous to that which occurs at puberty, when the ovary begins to functionate, the changed conditions in the ductless gland circuit sometimes causing pathological bleeding — the so-called "hemorrhages of puberty."

Looked at in this light, it can scarcely be said that the menopause in itself is never responsible for menorrhagia or metrorrhagia, although it cannot be too strongly emphasized that such an explanation for the bleeding should never be assumed until more dangerous anatomical causes are excluded. This applies especially, of course, to cancer, which so frequently manifests itself first at this age by excessive menstruation. In view of its great frequency and its great danger every case of excessive menstruation at or near the time of the menopause should be looked upon as cancer until proved to be otherwise.

Vasomotor Symptoms.— Most conspicuous among these are the peculiar *flushes* which affect usually only the head and neck, but which sometimes are general over the entire body. Associated with them are the *hot flashes* which come frequently over the entire body, although these too are usually most marked in the head and neck. When these come on, the patient experiences a sensation of stifling heat, so that in pronounced cases it is not unusual to be told that on a cold day the patient rushes to an open window for a breath of cold air. The duration of the flashes is commonly short, seldom more than a few minutes. Their frequency is very variable, both in different individuals and in the same individual at different times during the course of the menopause. When severe, they may recur a number of times a day, while in mild cases, on the other hand, they may occur only at intervals of many days. When mild in degree, the patient experiences only a sensation of warmth and flushing about the face. Associated with the flushes and the flashes, usually immediately following them, there is apt to be more or less copious *sweating*. This, however, is frequently absent.

Among other symptoms which are probably referable to the vasomotor system are vertigo, faintness, palpitation of the heart, epistaxis, vicarious bleedings from various parts of the body, cold hands and feet, etc. Some of these vasomotor symptoms are found in almost every case — certainly in over 80 per cent of all cases. The flushes and the heat flashes are the most frequent and most characteristic of the disturbances.

A satisfactory explanation of how these interesting phenomena are brought about is not possible in the present state of our knowledge. Like the other symptoms of the menopause, they are obviously due to the withdrawal of the ovarian secretion, but just how the absence of the latter affects the vasomotor system is not as yet fully worked out. A discussion of the relations between the vasomotor apparatus and the ductless gland chain will be found in Chapter XXII. Here it need only be said that the ovary is of course intimately associated with all the other organs which possess internal secretions, and that the latter are in turn closely related with the sympathetic nervous system, which embraces the vasomotor apparatus. These facts have been abundantly proved in the case of the thyroid and suprarenal especially. We are unable as yet to explain the workings of this intricate mechanism, but the knowledge we already possess enables us to recognize

an avenue of approach to the vasomotor centre from the ovary. The vasomotor centre, as is well known, is closely related with the heat centre or centres, and this fact led Byron Robinson to suggest that the heat flashes so often associated with the flushes are due to a coincident effect produced upon the heat centres. In the same way, the excessive perspiration sometimes noted has been explained as being due to a similar effect upon the sweat centre, which lies close to the vasomotor centre in the floor of the fourth ventricle.

In a study of the relation of menstrual vertigo to blood pressure, Sanes found that only 46 per cent of 102 cases had a pressure above 150, and only 30 per cent above 160.

As the result of a recent exhaustive study, Culbertson concludes that these vasomotor disturbances "represent an instability of arterial tension." He states furthermore that the ovarian deficiency of the menopause causes a relative oversufficiency of the pituitary and adrenals, thus causing a "vacillating hypertension." Since the diastolic pressure is not increased hand in hand with the systolic, there is produced an increase in the pulse pressure. To these fluctuations of the arterial tension, he ascribes the vasomotor symptoms of the menopause.

Psychic Symptoms.— In the mildest cases there appears to be no change in the disposition of the woman. In perhaps the majority of cases, however, there are psychic manifestations of one form or another, sometimes grave. Some women become peevish and irritable, others morose and depressed. In the most severe cases, which fortunately are rather rare, actual insanity may supervene, especially where there is a hereditary tendency. This may take any one of a number of forms, melancholia and paranoid conditions being most common in my experience, although the various maniacal conditions are not rare. This subject, however, will be more fully discussed in Chapter XV.

Nervous Symptoms.— Aside from the general nervous irritability, there are many possibilities as regards special symptoms referable to the nervous system. One of the most interesting of these, though not a very frequent one, is *tachycardia*. Knowing how constantly this phenomenon is associated with hyperthyroidism, one is tempted to believe that perhaps its occurrence at the climacterium is to be explained by a relative hyperthyroidism, as a result of the withdrawal from the circulation of the ovarian secretion. That the thyroid is intimately associated with the nervous system, and especially with the sympathetic, is well known, hence the tachycardia would seem to be due to a stimulation of the cardiac sympathetic nerves rather than an inhibition of the vagus. Palpitation of the heart is also frequently complained of, either with or without tachycardia.

Many patients complain, sometimes persistently, of sensations of *numbness* or *tingling* in various parts of the body, most often the upper extremities. Another frequent and troublesome symptom is *pruritus*, sometimes general and sometimes confined to the genitalia. In severe cases, the patient

is made quite frantic by the intolerable itching, which is often intractable to all the usual forms of treatment by nerve sedatives and local applications. In a recent case of my own, the pruritus was associated with and perhaps due entirely to a chronic urticarial eruption involving the entire skin surface, including the face and scalp. The irritability of the bladder so often seen at the time of the menopause appears in some cases to be entirely of nervous origin.

Last, but not least, in this group of symptoms, must be mentioned *headache* and *vertigo*. Especially annoying is the former. The headache of the menopause is not uncommonly vertical or occipital, and sometimes exhibits a peculiar periodicity. A patient recently under observation dreaded the approach of Sunday afternoon, which invariably brought with it a severe attack of headache. In such cases, of course, the psychic element no doubt plays an important part. In many instances the headache is accompanied by nausea or vomiting. The frequency of the attacks is very variable, as is their duration. In both these respects, the general nervous tone of the woman plays a part of much importance. In the case of delicate and highly neurotic women, there is, of course, a much greater susceptibility to frequent and stubborn headaches than in the case of women who are naturally more or less robust. What has been said of headaches applies in the main to vertigo, another common symptom of the menopause. Absent in some women, it is in others a symptom of great annoyance.

Other Symptoms.— Some form of gastric disturbance is frequently noted at the time of the menopause. Many years ago Kisch wrote of a *dyspepsia uterina,* especially frequent at this period. It must of course be borne in mind that for many cases of "indigestion" noted at this period there is some definite anatomic cause, such as gallstones, gastric or duodenal ulcer, or cancer of the stomach. Constipation is frequently noted, diarrhea being less common. The study and treatment of gastro-intestinal disorders at the climacterium offers a splendid opportunity for cooperation between the gynecologist and the gastro-enterologist or internist.

In some cases there is an increase in the sexual appetite, and it is said that some women who before this period have been sexually frigid, at this time become very passionate.

Skin eruptions of one form or another are occasionally seen at the time of the menopause, the most frequent form being urticaria. Acne may be observed, but it is much more rare than at the time of puberty.

Factors Influencing the Severity of the Menopause.— From the above recital of the principal possibilities in the clinical course of the menopause, one might get the impression that it represents a distinctly pathological period. Such, however, is not the case. It can not be too strongly emphasized that the menopause, like puberty, is one of the physiological epochs of a woman's life. Some one, with greater or less justification, has compared it with childbirth, which, while it is a physiological process, involves much pain and suffering. In the same way, it may be conceded that

the menopause also represents a physiological transition period, but it can not be denied that it may involve much annoyance and distress on the part of the woman. In some cases this is insignificant, in others distressing. The principal factors which influence the severity of the menopause are so well set forth by Currier that I can do no better than quote him. He says "All that tends to develop and strengthen the physical part of woman — to render her insensitive to the ordinary ills of life, to make her forgetful of self — is favorable to a normal menopause. Races and nations which are phlegmatic, cold and apathetic, women who are inured to out of door life and severe manual labor, savage and barbarous women, peasants, Germans, Scandinavians, and Russians, are apt to complain little of the experiences of the menopause; while the sensitive passionate nations, like the French, Spanish, and Irish, the highly organized, nervous, city bred women, women of fashion, women who fret and worry, are apt to experience the disagreeable and annoying features of the menopause." Speaking of the moderately troublesome cases, he says "The number of women who belong to this class is very large. It includes women who have had a stormy menstrual life, who have suffered much with dysmenorrhea, who have suffered much with anemia, headache, and constipation. It also includes women who have been addicted to venereal excesses, who have had frequent abortions, whose nervous systems have suffered frequent shocks, who have had great disappointments, whose lives have been a constant worry and unrest, also women who have undergone privation, overwork, and exposure of various kinds. Among them will be found many shopwomen, many prostitutes, women of fashion, women who bring up large families of children on very slender incomes, women who are hysterical and with whom the affairs of life are constantly going wrong, wives of farmers and mechanics who are frequently troubled to make ends meet."

Anatomic Changes of the Menopause.— All the anatomic changes demonstrable in various organs at the menopause are indicative of the universal retrogression which characterizes this period.

External Genitalia.— Marked atrophic changes are seen in the tissues of the *vulva*. The fat of which the labia are so largely made up disappears almost entirely, so that they become little more than two long skin folds, so flat in many instances as to be scarcely noticeable. The hair on their outer surfaces becomes gray and straggly. As a result of the atrophy of the labia majora, the labia minora become relatively more prominent, as in the child, even though they also undergo more or less wasting. The clitoris becomes very small, the glans clitoridis being often scarcely demonstrable in the bifurcation of the labia minora. As a result of the so-called senile atrophy, with its attendant thinning of the epithelial layer, the mucous membrane of the vulva loses its velvety, vascular appearance, and becomes thin, pale, and transparent looking, giving the surface a rather pasty appearance. Patches of catarrhal inflammation are often seen mottling the surface (senile vulvitis). The meatus urinarius is often granular looking, and not infre-

quently is everted. The mons veneris, like the labia majora, becomes low as a result of the disappearance of its fat.

The *vagina* becomes narrow and contracted, the result of the same process of senile atrophy, in which there is a replacement of parenchymatous by interstitial tissue. Annular lines of contraction are frequently noted, and occasionally the lumen of the canal may be almost or quite obliterated. The fornices of the vagina become narrow and conical, the apex of the cone corresponding to the cervix. The vaginal mucosa, like that of the vulva, becomes thin and atrophic.

Fig. 26.— Senile Endometrium from a Patient Aged 49 Years.

Internal Genitalia.— The *cervix uteri* becomes very small and short, often feeling like a small button set in the top of the vaginal fornix. The external os, especially in nulliparous women, becomes so narrow as scarcely to be distinguishable. The *corpus uteri* shares in the general atrophic change, becoming small and hard. The muscular structure of the myometrium is to a considerable extent replaced by connective tissue.

Especially noteworthy, however, are the changes in the *endometrium*, which becomes thin and avascular. The glands lose their full tortuous appearance and become straight and narrow. (Fig. 26.) The increase in the connective tissue often causes an encroachment upon the glands, some-

times even obliterating their lumina, and occasionally causing small glandular retention cysts. The epithelium lining the utricular glands, as well as that covering the surface, becomes low and cuboidal. In extreme cases, it is almost flat, like squamous epithelium. This transformation is considered by some to explain the occasional occurrence of squamous cell carcinoma of the corpus uteri, a few authentic cases of which have been recorded.

The stroma, normally made up of round or oval cells, shows the presence of increasing numbers of spindle cells. Under the microscope these can usually be seen traversing the field in long streaky looking bands. In very old women, the stroma consists of what is virtually ordinary connective tissue.

The *fallopian tubes* also participate in the retrogressive processes of the menopause, becoming shorter and thinner. The fimbriae disappear or become very inconspicuous, as do also the longitudinal rugae in the mucosa. Miscroscopically the epithelium is seen to have undergone a flattening similar to that observed in the uterus, while the muscle tissue in the walls is in large measure replaced by connective tissue.

In the *ovaries* striking changes are observed at and after the menopause. While occasionally the size of the ovary is not much changed, in the majority of instances the organ is much diminished in size, perhaps to only one half or one third of its original size. This gives it a peculiar beady feel on bimanual examination. The surface is not glistening as in the case of the ovary of the young woman, being now of an opaquely white appearance. The peculiar wrinkling of the surface so generally noted at this time reminds one of the appearance of the surface of a peach stone. When the senile ovary is cut across, its surface is found to be firm and dense, owing to the preponderance of connective tissue. Numerous cicatrical islands, usually of rather scalloped appearance, mark the sites of former corpora lutea. The differentiation between cortex and medulla becomes well marked. Fig. 27 illustrates the appearance of a section of the senile ovary.

Other Changes.— The breast glands, so intimately bound up with the generative organs physiologically, become small and atrophic. Sometimes the breasts not only do not diminish in size, but may even become larger, but this is due to a marked deposition of adipose tissue. The glandular tissue, however, undergoes atrophy, the acini being smaller and more discrete.

As for the general appearance of the woman, the only conspicuous alteration — and even this is not constant — is a tendency to a general *increase of the adipose tissue*. The figure therefore is usually more rounded and matronly, and often actual obesity develops. In other cases, on the other hand, the woman loses weight, and if thin before, becomes even more spare and angular.

Diagnosis.— In the great majority of cases, there is no difficulty in recognizing the occurrence of the menopause. As a rule the woman who

has reached the age at which it usually occurs is prepared for its incidence, and if not, she is apt to receive due warning in the form of the vasomotor flushes which so often precede the actual cessation of menstruation. When the latter phenomenon is noticed, therefore, it excites no great concern, and many women do not even consult the physician. In a certain percentage of cases, however, it becomes necessary to decide whether the cessation of menstruation is an indication of the onset of the menopause, or whether it

FIG. 27.— SENILE CHANGES AS SEEN ON TRANSVERSE SECTION OF OVARY (patient aged 48 years).

Note dense, well defined cortex, as contrasted with the medulla. The hilum is seen below and to the right.

is only a temporary amenorrhea due to some other cause. It is not always easy to make this differentiation.

The condition which is most apt to be confused with the menopause is the amenorrhea of pregnancy. Every physician must confront this problem frequently, and mistakes are not uncommon. Many a woman who becomes pregnant after the age of 40 thinks she is entering upon the menopause, until time or the physician disillusions her. On the other hand, it not infrequently happens that the amenorrhea of the menopause is mistaken for pregnancy, especially in the case of women who are very desirous of having

children. The problem in such cases is made much harder by the fact that the natural tendency of the menopause is to make the woman stouter than formerly. Many cases of pseudocyesis or "spurious pregnancy" are of this type. Only recently I had occasion to examine a lady of 42, who since her marriage at the age of 35 had been very anxious to become a mother. She had not menstruated for six months, the abdomen had increased very much in size, and she had even, she said, had some nausea at times. She considered herself pregnant, an opinion in which her physician concurred, although no examination had been made. She had made all her arrangements for the expected confinement, and it was difficult to convince her that she was not pregnant. Her uterus was not enlarged and was of the infantile type. Many similar cases might be cited. When menstruation has been absent only a month or two the diagnosis can not usually be made with certainty. In later stages, however, pelvic examination, with especial reference to possible enlargement of the uterus, will usually clear up the diagnosis. Other points of differentiation, such as absence of the fetal heart sounds, need only be mentioned.

Treatment of Menopausal Disturbances.—General Measures.—The higher the standard of general health and resistance with which the woman enters upon the menopause, the better her chance of passing through it with a minimum of discomfort. It is scarcely necessary, therefore, to dwell at any length upon the importance of such factors as care in diet, proper sleep, bathing, avoidance of constipation, and, especially, the avoidance of worry and anxiety of any sort. Strict insistence by the physician on the carrying out of these measures and an intelligent coöperation on the part of the patient will do much to mitigate the suffering of the woman who is passing through this trying period.

Treatment by Drugs.— There are many women who pass through the menopause with little or no disturbance, either physical or psychic, so that the administration of drugs or other remedial measures is never called for. On the other hand, as we have seen, it is common to find women suffering with more or less distressing symptoms. The clinical picture is so different in different women that a rational treatment of the condition must adapt itself to the individual needs of the particular case. Indeed, it may be said that, so far as drugs are concerned, the treatment of the menopause is purely symptomatic. A few suggestions may be made as regards the treatment of some of the more common symptoms.

Hemorrhage.— The important fact to bear in mind, in connection with climacteric hemorrhage is, of course, the frequency with which it heralds the invasion of uterine cancer. The physician owes it to the patient to suspect the development of cancer whenever such abnormal bleeding is present. Only the physician who has "cancer on the brain," as Carstens puts it, will be likely to detect the disease in a stage which still offers hope of cure. The treatment of hemorrhage at the climacterium should be primarily surgical, even though there is no gross evidence of cancer. Explora-

tory curettage may reveal the presence of adenocarcinoma of the body of the uterus, or of some benign surgical lesion, such as submucous myoma or polyp.

If no anatomic cause for the bleeding be found in the pelvis, either in the uterus or in the adnexa, treatment by various drugs is frequently resorted to. Among those most commonly employed are ergot, hydrastis, pituitary extract, apiol, and stypticin. The treatment of climacteric hemorrhage will, however, be more fully discussed in Chapter XXII.

Nervous Symptoms.— For the *"nervousness"* which is so frequently complained of at the menopause, the remedies most commonly resorted to, and probably of the greatest value, are the various bromids. Sodium or potassium bromid in rather moderate doses (gr. x or gr. xv three times a day), either alone or in association with other drugs. may be recommended both for the nervous irritability and for the headache and neuralgia so often complained of. When the latter symptoms are very severe, however, relief may be more readily given by the administration of aspirin (gr. v to gr. x every 4 hours) or the various coal tar products, such as acetanilid (gr. iii to gr. v every 4 hours), or acetphenetidin (gr. v to gr. x every 4 hours). The latter group of drugs, on account of their well known tendency to cause cardiac depression and other untoward effects, must of course be administered guardedly, and should be combined with appropriate doses of caffein.

Another troublesome symptom is *insomnia.* In addition to various general measures, such as hot baths at bedtime, avoidance of excitement, plenty of fresh air, etc., drugs are occasionally indicated, although their administration should be as restricted as it is possible to make it. Here again the bromids of sodium, potassium, or strontium, are of value. Another useful drug is veronal, given in doses of from five to ten grains several hours before bedtime, preferably with hot milk. Instead of veronal, one may employ trional, sulphonal or paraldehyd.

In the comparatively rare cases where an actual mental disturbance supervenes, the treatment, of course, passes over to the realm of the psychiatrist. Frequently it becomes institutional, although the outlook in cases of menopausal insanity is, in my own experience, relatively favorable.

Vasomotor Symptoms.— The vasomotor *flushes* and *sweats,* and the *flashes of heat* which have already been described as perhaps the most characteristic phenomena of the menopause, are entitled to separate, if brief, consideration. Taken as a group, it may be said that drug treatment of these symptoms is less satisfactory than in any other group of phenomena observed in the patient at the menopause. On the other hand, as we shall see, it is in this group that the most striking results of organotherapy are noted. The treatment of these disorders by organ extracts is discussed in Chapter XXVI.

Of the drugs used for these vasomotor disturbances may be mentioned the bromids, arsenic, ergot, and belladonna. Except in the case of bromids, it is difficult to suggest a pharmacodynamic basis for the employment of

these drugs. Arsenic, usually administered in the form of Fowler's solution, is said to be especially indicated when the patient is anemic.

Engelhorn has recently reported good results from venesection in a number of cases in which menopausal symptoms were troublesome. The annoying "hot flashes," sensations of heat, and the attacks of sweating and redness were relieved. This procedure, indeed, had been recommended by Hufeland as far back as 1839. Engelhorn never withdraws more than 100 c.cm. of blood at one time, although in a few cases it was necessary to repeat the venesection.

Local Symptoms.— The most frequent of the local symptoms of the menopause is the so-called *senile vulvovaginitis,* characterized especially by a troublesome leucorrhea, sometimes slight hemorrhage, and frequently pruritus vulvae. The latter may be noted even when there is no local alteration in the vulvovaginal mucosa. It is often a most annoying and perhaps agonizing symptom. It need scarcely be said that when pruritus is due to some local cause, whether this be vulvovaginitis, eczema, pediculi pubis, etc., the local condition must receive direct treatment. If it can be cured, the pruritus will usually disappear unless extensive tissue changes have been produced. In the latter case, it may persist.

Special emphasis must be laid upon the importance of careful examination of the urine, particularly for the presence of sugar. More than once in my experience a persistent pruritus has thus led to the diagnosis of a previously unsuspected diabetes.

In the so-called neurotic cases, however, no local cause can be discovered. Relief of the symptoms is often an extremely difficult matter, as one may judge from the number of remedies which have been suggested. One of the simplest and best, in my experience, is carbolic acid, applied as a lotion in the strength of from two to five per cent. It may be combined with a little glycerin or alcohol, or it may be applied as an ointment.

The following prescriptions are suggested by Kelly:

℞ Pulv. camph. .....gr. iv
Menthol. .....gr. x
Ac. carbolic .....gr. xxv
Lanolin. ..... ʒ i
M. S. Apply externally.

℞ Cocain hydrochlorid .....gr. vi
Lanolin. ..... ʒ i
M. S. Apply externally.

℞ Liq. plumb. subacetat. ..... ʒ ii
Tinct. opii ..... ʒ ii
Liq. calcis ..... ʒ vi
M. S. Apply externally.

Finally, mention must be made of the efficacy in the treatment of these cases of the powerful new therapeutic agent, radium. Many cases which

have resisted other forms of treatment are promptly cured by one or two applications of radium.

ORGANOTHERAPY.— This subject is fully discussed in Chapter XXVI.

XIII

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CHAPTER XIV

THE HYGIENE OF THE MENOPAUSE

General Measures.— Other things being equal, the woman who approaches the climacterium in good physical health is much less likely to suffer severe disturbances than the one who arrives at this period worn out by physical disease, many childbirths, domestic cares and anxieties, and other such causes. It seems scarcely necessary, therefore, to emphasize the importance at this epoch of such factors as fresh air, plenty of rest, proper regulation of the bowels, etc. Sociologic considerations may make it impossible to secure all these desiderata in full measure, but the ideal should be approximated as closely as possible.

Of especial importance is the avoidance of worry and anxiety. The brunt of the menopausal storm seems to fall upon the woman's nervous system, and this should be spared in every possible way. Members of her family should be urged to show her every consideration at this trying period, when even pronounced temperamental changes may make themselves evident. Owing to the instability of the nervous system at this period, influences which at other times would be without effect may at the menopause result in more or less troublesome psychopathies. This is especially true in the case of women with a neurotic taint (Chapter XV).

The Education of Women as to the Danger of Cancer.— By far the greatest danger to be feared at or near the time of the menopause is the development of cancer of the uterus. The most important hygienic consideration at the climacterium, therefore, is the education of women as to the danger signals of this dread disease. Foremost in importance among these is uterine bleeding, which is the initial symptom in the largest number of cases. Even when, as sometimes happens, its appearance is preceded by that of a watery leucorrhea, it is the abnormal bleeding which is most likely to direct the woman's attention to the possibility of serious trouble.

Unfortunately, there is prevalent among women a belief that menstrual excess is often a concomitant of the normal menopause, and hence this symptom is frequently disregarded until the disease has reached a hopeless stage. In other cases, again, even though the woman herself be sufficiently enlightened to suspect the development of uterine cancer, the dread of having this suspicion confirmed deters her from seeking medical advice.

For this reason, I have always felt that in all cancer educational work, whether carried on with individual women by individual physicians, or on a large scale by organizations devoted to the purpose, emphasis should be

laid upon the fact that cancer is by no means the only cause of menopausal bleeding, and that most of the other causes offer far more encouraging prospects of cure than cancer. Furthermore, it should be urged that even when cancer is present, it is often curable in its early stages, and that certain cases of cancer, i. e., carcinoma of the fundus, are often amenable to cure even when they have been present a relatively long time. In other words, the message should be one of hope and encouragement rather than one of despair, so that women may come to feel that there is a vitally important incentive for watchfulness at this period.

The Responsibility of the Physician.— Not always, however, is the patient herself responsible for the fatal delay in the recognition of uterine cancer. In spite of the fact that the ominous significance of climacteric bleeding has been repeatedly emphasized by innumerable authors, it is unfortunately true that not infrequently, even in this day, it is the physician who is to blame for disregarding this symptom when it is reported to him by the patient. The proper attitude of the practitioner toward suspicious menopausal hemorrhage is so well expressed by Thornton that I cannot do better than to quote him verbatim, as Cullen has done:

" How is an early diagnosis to be made? Clearly, by neglecting no menstrual departure from the normal, however trivial it may at first sight appear, but encouraging the patient to at once accurately describe symptoms, and above all insisting in the most determined manner on a local examination. Here it will be apparent that I, as a consultant, appeal for help to the great body of those who are now listening to my remarks, to my professional brethren engaged in general practice. I, in common with those situated as I am, too seldom have an opportunity of diagnosing early, because the majority of the patients come to us too late, when the disease had already advanced nearly, or quite, beyond the limits of surgical aid. Let me then appeal to all engaged in family practice who listen to me here, and to that larger body who may read my words when reproduced in the medical journals, to sternly cast aside that too great modesty, or that tendency to treat as trivial small symptoms, and to at once take alarm about, and carefully investigate, every case in which there is brought to their notice an abnormality in menstruation, or a vaginal discharge of any kind, however trifling. A very grave responsibility lies at the doors of the medical profession for the small progress made in the early diagnosis of uterine cancer and its successful treatment. How constantly is the consultant told: 'I mentioned it to my doctor weeks or months ago, but he said "Oh, it is nothing; I will send you a little medicine or a little injection," and never even suggested any internal examination, so I did not like to trouble him again until the pain became so bad or the discharge so troublesome, and then he examined me and said I must have special advice at once.' Invaluable weeks or months gone, and then the verdict of the consultant, 'It is not a case for operation,' which really means 'You have come too late,' but cannot be so candidly expressed, because he must guard the

reputation of his professional brother. I admit that the false modesty of the patient, especially in some classes of society, makes the position a difficult one, especially for the young family doctor, but let me implore you all to wake to what is at stake, and to be firm in your demand for an examination, and if you have any doubt after such an examination, to urge that the patient should at once seek the advice of some one who has larger opportunities than yourself for forming a sound opinion. I will go one step further, and ask you, if there should be any to whom such a temptation comes, never to go on treating a case in which there is a shadow of doubt, either because you doubt or because you want practice; if the case is susceptible of treatment at all, it is only surgical treatment which can avail, and that of so severe a kind that it requires the knowledge of the specialist, if ever any disease did or does require special knowledge and special skill in operative treatment."

XIV

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CHAPTER XV

PSYCHOPATHIES OF THE MENOPAUSE

Incidence.— The various psychoses of the menopause constitute an important group of cases. I have been unable to find a statistical study of this subject upon any large number of cases in this country. In England, however, a thorough investigation of the menopausal psychoses has been made by R. Percy Smith, who presented his results at the meeting of the Section of Neurology and Psychological Medicine of the British Medical Association in 1912.

According to Smith, the statistical tables of the Lunacy Commissions for England and Wales state that the climacteric is a cause or an associated factor in 8.2 per cent of all the cases of female patients admitted to public and private asylums and registered hospitals in the years 1907, 1908 and 1909. It is shown that mental disorder at the climacteric occurs more frequently in private patients than in those of the pauper class, the figures for the former being 11.2 per cent of admissions and for the latter 7.8 per cent. This Smith explains by the fact that with the former class such factors enter as idleness, introspectiveness, etc.

In 1871 cases of insanity in women which came under Smith's personal observation at Bethlehem Hospital, the number of cases in which the menopause was considered to be a cause or an associated factor was 118, or 6.3 per cent. Baugh's figures, based on 510 female patients admitted to the Gartloch Mental Hospital for Glasgow, during a period of four years, indicate that only 3.1 per cent of the total admissions were to be classed as climacteric insanity.

Influence of the Marital State.—In 219 cases of climacteric insanity studied by Smith at the Bethlehem Hospital, and in private practice, 34.5 per cent were single women. Of 102 cases studied by Goodall 42.1 per cent occurred in single women, while Craig found that 21.5 per cent of 120 patients with climacteric insanity were single. From these figures it might appear that the psychoses affect married women much more frequently than the unmarried. Allowance must be made, however, for the much greater number of married than of unmarried women in the population at the climacteric age. Thus, as Smith points out, in England there is only one single woman to about six married women or widows in the decade from 45 to 54 years, so that the actual incidence of climacteric insanity is really greater in single women than in the married.

Age of Patients.— Menopausal insanity may obviously occur at any

age at which the menopause occurs. Extremes of 38 and 61 years are mentioned by Smith. The average ages at which climacteric insanity was noted by Smith, Goodall, and Craig were 48.9, 46.7 and 47.5 respectively.

Influence of Heredity.— In 101 private cases Smith found a family history of insanity, neuroses, alcoholism, and drug habits in 58 per cent. In addition, in 6 cases a child of the patient had previously broken down mentally, or had been congenitally imbecile. These figures indicate that in a large proportion of cases the menopausal crisis acts simply as the exciting cause of insanity in patients who already are strongly predisposed to it.

The figures of Smith, it must be repeated, are based on private cases alone, and the greater ease with which adequate histories can be obtained in such cases may explain the rather startling percentage of cases in which heredity plays an influential factor. A similar study of pauper cases, made from figures of the Lunacy Commissions for England and Wales, shows that in only 29 per cent was there obtained a history of heredity in insanity, epilepsy, neuroses or alcoholism.

Correlated Causes.— The tables just quoted further indicate that in 39 per cent of the cases of menopausal insanity, the climacteric alone was given as a cause. In 19 per cent sudden or prolonged mental stress was given as a contributing cause, while in 7.6 per cent alcoholism was given as a causative factor.

Previous Attacks.— In a review of 118 cases from the Bethlehem Hospital, Smith found that 41, or 34.7 per cent, had suffered with previous attacks of mental disorder. In 101 private cases, the percentage was 33. These figures indicate that climacteric insanity is not to be looked upon as a special form of insanity, but that the climacterium, like any other crisis, merely breaks down the resistance of an unstable mind. This view is supported by no less an authority than Kräpelin.

Types of Mental Disorders.— The manifestations of climateric insanity are quite protean. As Sir George Savage remarks, "any normal symptom, bodily or mental, which may occur with the menopause, may be so exaggerated as to become morbid." The psychic disorders especially are numerous and varied. Not infrequently they are strongly sexual in character.

Sir Felix Semon lays stress on the frequency with which sensory neuroses of the throat are noted at this period. They are never of the anesthetic type, paresthesia or neuralgia being the usual manifestations. They may either precede or be associated with the menstrual irregularities of the menopause. Sensations of constriction in the throat, or a feeling that the food stops in the throat, are quite common.

The prodromal symptoms are summed up by Goodall and Craig as follows: "Insomnia, alterations in temper, neurosis, noises in the head and ears, and deafness, hallucinations of the various senses; suspicions, jealousies, false accusations; failure of attention, impairment of memory; sexual perversions (erotism, frigidity, masturbation, etc.)."

The depressed or melancholic forms of insanity are the most frequent at the menopause. Not infrequently they assume a suicidal tendency. Of 219 cases, Smith found that 66 per cent were classed as melancholia. Any or all of the usual manifestations of the latter may be observed — the depression and lack of energy, inability to concentrate thought or attention, insomnia, feeling of worthlessness, headache, desire for death, etc.

Maniacal insanity is much less common, but may occur. Paranoia was found by Goodall and Craig in 9.8 per cent of the cases at the Bethlehem Hospital, in 14.1 per cent at Wakefield. Smith found it in about 16 per cent of his cases. A large number of the delusional cases have a strongly sexual basis.

Illustrative Cases.— A very brief sketch of a few personal cases will illustrate some of the types assumed by climacteric insanity:—

1. A woman of 48, unmarried, was convinced she was pregnant because she had had one coitus many years before. Nothing could shake her conviction, even after a myomatous uterus, about the size of a small cocoanut, had been removed.

2. A woman of 44, who had recently passed through a severe attack of typhoid fever, and who had previously exhibited signs of beginning menopausal mental disorder, believed that enemies were endeavoring to steal her two children, whom she therefore kept under constant watch. She could hear her supposed persecutors plotting under her window at night.

3. A woman of 49, a widow, who had hitherto been temperate in her religious beliefs and practices, became quite maniacal. Hour after hour of day and night was spent in loud prayers before images of the saints.

Smith mentions the following cases, among a number of others:—

1. A woman of 49, with the delusion that she smells, and is decaying, and is rotten with syphilis, asks her husband to shoot her. Committed suicide by hanging.

2. A married woman of 46, who developed the delusion that her husband was poisoning her "per vaginam" during intercourse, that he was unfaithful to her, and would kill her, and that her daughter was immoral. This was associated with eroticism, the patient stripping herself and demanding sexual intercourse.

Prognosis.— Roughly speaking, it may be said that something like one half the cases recover. Clouston found the proportion to be 57 per cent in 228 cases, but Goodall and Craig give it as 35.29 per cent in the cases at the Bethlehem Hospital, and 40.8 per cent at Wakefield. Smith's cases give a percentage of 42.3 per cent of recoveries. It is scarcely necessary to say that the prognosis depends in large measure upon the type of mental disorder which attacks the patient. The paranoiac cases, of course, become chronic.

XV

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CHAPTER XVI

RELATION OF MENSTRUATION AND OVULATION

Historical.— Ever since the discovery of the human ovum by von Baer in 1827 there has been much discussion as to the relation, if any, which exists between the phenomena of menstruation and ovulation. The older writers appear to have assumed quite generally that the menstrual bleeding is the result of the general pelvic congestion believed to accompany the ripening of the follicle and the escape of the ovum. I believe that it was Matthews Duncan who stated that the menstrual flow might be compared to the red flag hung outside the door of an auction room, showing that something is going on inside.

As we have already seen, the earlier writers, like Freind and Astruc, believed that menstruation is induced by ovulation, and that in the event of fertilization of the ovum, the menstrual blood is retained for the nourishment of the embryo. The occurrence of graafiian follicles had been described by de Graaf, after whom they were named, as early as 1665. It was not until 1839, however, that Gendrin asserted the dependence of menstruation upon spontaneous ovulation. Negrier, in 1831, and Lee, of London, in the same year, are said to have already described the interrelationship of these two phenomena. Brierre de Boismont, Bischoff, and Pouchet all believed in the dependence of menstruation upon follicular rupture, i. e., upon ovulation.

This same relationship was assumed in the well known theory of Pflüger, which was published in 1865, and which enjoyed quite general acceptance, virtually up to the beginning of the present century. According to this theory the stimulus for the menstrual congestion is excited reflexly through the medium of nerve channels by the ripening of the follicle. The rupture of the follicle with the discharge of its ovum was considered to take place during or just after the menstrual bleeding. Somewhat similar views were entertained by Leopold and his pupils, Mironoff and Ravano.

Relation of Estrus and Ovulation in Lower Animals.— Not a great deal of light has been thrown upon this question, as it concerns human beings, by a study of estrus and ovulation in the lower animals. Most of our knowledge concerning these matters has been gained from investigations upon domesticated animals or upon wild animals in a state of captivity. The studies of Heape and others seem to show that in the lower animals, at any rate, ovulation is not necessarily coincident with estrus. On examining the pelves of forty-two monkeys during estrus, Heape found

evidence of ovulation in only two. In the same way, histological examination of the ovaries of bats at the time of estrus shows that they are fallow, and that ova do not ripen until several months afterward, the spermatozoa being carried into the genital tract during the intervening period.

The most recent experimental work on this subject is that of Marshall and Runciman, whose investigations, like those of Heape, indicate that there is no relationship between ovulation and the estrous cycle. They point out that most animals ovulate after the pro-estrum is over, so that corpora lutea are not necessarily found when "heat" begins. Furthermore, they call attention to the fact that in the cat, the rabbit, and certain other animals, ovulation takes place ordinarily only after sexual intercourse. Corpora lutea are not found, therefore, in the absence of the male, and yet the female rabbit and cat may, in this condition, experience recurrent periods of "heat."

The studies of Marshall and Runciman were made upon four bitches. The dates of periodic sexual activity were determined by a period of preliminary observation. The effect of ovulation, or rather of its non-occurrence, upon the expected recurrence of estrus was determined by rupturing all the visible follicles in both ovaries at definite periods preceding estrus. The experiments indicated that "the occurrence of heat in dogs does not depend upon the presence of mature (or nearly mature) graafian follicles in the ovaries. It is equally evident that it is not dependent upon corpora lutea. It must be supposed, therefore, that the ovarian factor in the recurrence of "heat" resides in some other ovarian element or combination of elements. The ovarian interstitial cells are possibly concerned in the process, but cyclical changes in the condition of these cells have not so far been observed in the dog's ovaries. The view which has generally been maintained, that the ripening of the graafian follicles and the onset of menstruation or heat stand to one another in the relation of cause to effect, must be finally abandoned. It is probable that both series of changes are effects of some more deep seated ovarian phenomenon."

Although the results of Marshall and Runciman are very suggestive, it would seem that the material on which the study is based is too meagre to allow of any very emphatic generalizations. Their methods, moreover, do not seem to be free from objection. They state that "the ovaries were exposed, and each follicle, showing on the surface, was pricked by a knife or needle." It would seem to be very difficult, by their method, to exclude the possibility that one or more follicles may be left behind or may develop and ovulate subsequently to the operation.

Attention may again be called to the studies of Fraenkel, Loeb, Halban, and others, which have already been described at some length in a preceding chapter (Chapter VII). It will be recalled that the results obtained by these various investigators were so unlike that they permit of no definite conclusions, on experimental grounds, as to the exact relation between menstruation and ovulation.

CLINICAL OBSERVATIONS ON RELATION OF MENSTRUATION AND OVULATION

General Considerations.— The numerous clinical reports which have been made on this subject throw even less light on it than do the experimental studies which have been made. The contradictory nature of these observations is in large measure due to the unreliability of the evidence as to the exact date of ovulation. For example, the mere presence of a corpus luteum in the ovary cannot, as has so frequently been assumed, be looked upon as indicating that ovulation has occurred just previously. Again, many authors have confused the problem of whether menstruation is caused by ovulation with the totally different question of whether or not these two phenomena occur synchronously.

Many of the observations bearing on these problems are rendered quite valueless by such considerations as these. At the present time it cannot be said that clinical investigations have offered conclusive evidence either for or against the theory that there is a definite relationship between the functions of ovulation and menstruation. Many suggestive facts have been brought out in this connection, however, which when taken together with the results of histological and experimental studies, have thrown much light on this important problem. It may be of interest to review some of the more important observations which seem to bear on this question.

Ovulation Before Puberty.— Numerous cases are recorded in which ovulation, demonstrated by pregnancy, has occurred before the onset of the menstrual function. It is said that among some savage tribes it is considered a crime for a girl to menstruate before she is married, such marriages often resulting in pregnancy before the onset of the menstrual function.

The occurrence of pregnancy in a woman of thirty-two who had never menstruated is reported by Ahlfeld. The same author reports a case of extra-uterine pregnancy in a girl of thirteen who had never menstruated. De Sinéty reports the case of a woman of thirty-eight who had never menstruated, although the ovaries were normal. Graafian follicles were present, as well as corpora lutea, showing that ovulation had occurred. As a matter of fact, corpora albicantia and a corpus luteum were found by Runge in the ovary of a newborn child.

Ovulation During "Dodging Period" of Puberty and Menopause.— There are few physicians who have not noted the occurrence of pregnancy during the "dodging period" of either puberty or the menopause. The physiological amenorrhea so frequently observed at these periods is not always easy to distinguish from the amenorrhea of pregnancy. Many delicate and perplexing problems are thus presented to the physician. They are rendered more difficult by the averseness of most of us to recommend pelvic examination in the case of young girls, and, on the other hand, by the perfection with which at least the subjective symptoms of pregnancy may be

mimicked in the cases of pseudocyesis so frequently observed at the age of the menopause.

Ovulation After Menopause.— Cases are occasionally observed in which pregnancy occurs after the menopause. As a rule the impregnation in these cases occurs within a year of the last observed menstrual period, but occasionally a period of years may elapse between the cessation of menstruation and the occurrence of pregnancy.

A rather remarkable case of this kind is that reported by Buckle. His patient was fifty years old, and had had seven children, the last two (twins) having been born fifteen years previously. A year after this childbirth, menstruation returned, but with considerable irregularity. In another year it ceased entirely. Eleven years later she was delivered of a boy. Strange to say, menstruation returned about a year after this childbirth, and had been occurring regularly every month up to the time of the report, when the patient had reached the age of fifty.

Ovulation During Pregnancy.— There has been some discussion of whether or not ovulation occurs during pregnancy, when amenorrhea is, of course, the rule. A satisfactory solution of this question would be of value in determining whether ovulation and menstruation go hand in hand. Unfortunately the studies so far made are more or less contradictory. Ravano, working in Leopold's clinic, found that follicles are continually and regularly undergoing ripening during pregnancy, and that ovulation occurs in about 5 per cent of all cases. In this, however, he is contradicted by Seitz, who states that ovulation never occurs during pregnancy.

Ovulation During Lactation.— Another opportunity of studying the relation or lack of relation between menstruation and ovulation is afforded during the period of lactation. As is well known, menstruation is absent during lactation in a large proportion of women (see Chapter XVII). Nevertheless it is common to observe the occurrence of pregnancy during this period. Chrobak records the case of a married woman who did not menstruate until after her fourth childbirth.

More remarkable are the cases of Roudellet and Joubert. The first speaks of a woman who had twelve children and the second of a woman who gave birth to eighteen children, although neither had ever menstruated. Meigs described the case of a woman with ten children, who had not menstruated since marriage, having always become pregnant before the return of menstruation after confinement.

Ovulation During Pathological Amenorrhea.— As is well known amenorrhea is a symptom of numerous pathological conditions, especially those of a debilitating nature, such as anemia, tuberculosis, lead poisoning, etc. (Chapter XVIII). In spite of the frequent absence of menstruation in such conditions, ovulation and pregnancy not infrequently occur. The incidence of pregnancy in women suffering with pathological amenorrhea is less than in normal women, but this fact is evidently due to other factors than the non-occurrence of menstruation.

A recent case of my own is of interest in this connection. The patient was a young married woman of twenty-three, who consulted me on account of amenorrhea of two months duration. She had gained twenty-five pounds in weight in the preceding few months. A diagnosis of adiposogenital dystrophy was made, the uterus being small and there being no evidence of pregnancy. Three months later she consulted me again, not having menstruated in the interval. Examination at this time showed the uterus enlarged and evidently the seat of a two months pregnancy, which diagnosis was confirmed by the subsequent delivery. In other words, this woman had become pregnant during the period of pathological amenorrhea associated with the adiposogenital dystrophy.

Evidence from Operative and Postmortem Findings.— Many of the older observations coming under this head are more or less invalidated by our newer knowledge of the life history of the graafian follicle and corpus luteum, so that they now possess little more than a historic interest. This is true, for example, of the conclusions arrived at by Lawson Tait from a study of twenty-eight specimens removed by him, and divided into three groups. He said "The first (three cases) show that menstruation and ovulation are concurrent; the second (seventeen cases) that ovulation is certainly progressive and not coincident with menstruation; in the third (eight cases) the findings are doubtful. . . . The weight of evidence, however, is certainly in favor of the view that the two functions of ovulation and menstruation are most likely quite independent in the human female, although there are reasons for believing that primitively, at any rate, the most usual period for ovulation in woman was during a definite estrum and succeeding a pro-estrum, as in some of the lower animals."

Girdwood reported the case of a girl of sixteen who had menstruated six times and in whom there were five distinct scars on the ovaries. He speaks also of a case in which he observed thirty-five scars in a patient who had menstruated thirty-six times, and of one who had menstruated twenty-four times and in whom twenty-two scars were found.

Bischoff from a study of operative and postmortem findings, concludes that the time relationship between the bursting of the follicle and the occurrence of menstruation is subject to considerable variation.

Zinke described a case in which a fully developed graafian follicle was found at the postmortem upon a woman who had died in the middle of the intermenstrual period, an observation more or less in accord with the conclusions of recent histological methods of study, as will later be shown.

Hyrtl found an ovum at the uterine end of the fallopian tube in a woman who had died three days after menstruation.

Leopold and Mironoff reported forty-two cases, in thirty of which menstruation and ovulation coincided, while in the remaining twelve menstruation occurred without ovulation. Arnold collected fifty-four similar observations, in thirty-nine of which ovulation and menstruation were said to

have occurred synchronously. Somewhat similar results have been reported by Williams and by Reichert.

Summary of Clinical Evidence.— The clinical evidence which has thus far been brought forward appears to prove beyond doubt that ovulation can occur without menstruation. It throws little light, however, on the much more difficult question of whether or not menstruation can occur without ovulation. It is easy enough to determine the occurrence and the date of menstruation, but it is not so easy to determine the occurrence, much less the exact date, of ovulation. It is this consideration which makes difficult the study of the relation of menstruation and ovulation, and especially of the time relation between the two functions. It is only by careful histological studies of the ovarian elements at different periods of the menstrual cycle that we can expect to arrive at any intelligent conception of the chronological relation between menstruation and ovulation.

HISTOLOGICAL STUDIES ON RELATION OF OVULATION AND MENSTRUATION

General.— By far the most valuable and trustworthy evidence as to the relation between these two phenomena is that which has been yielded by histological methods of study. These methods embrace two principal lines of investigation, (1) embryological studies, and (2) histological studies of the ovary.

Evidence from Embryological Studies.— The determination of the exact time at which ovulation occurs in relation to the menstrual cycle is a matter of the greatest importance to both obstetricians and embryologists. More accurate knowledge along this line would aid the former in fixing the date of fertilization and in estimating the duration of pregnancy, while embryologists, on the other hand, would find a great difficulty removed in the task of estimating the exact age of the fetus. Even when the date of a single fruitful coitus is known, we cannot form an accurate idea of the exact time at which the ovum was liberated from the follicle, owing to the uncertainty as to the time elapsing between ovulation and the fertilization of the ovum.

The classic contribution of Reichert in 1868 led to the acceptance for many years of the theory that ovulation precedes menstruation. His report was based on the study of a very early ovum obtained two weeks after menstruation in a woman who had committed suicide. A well developed corpus luteum was found in one ovary. A further study by Reichert on the condition of the ovaries during menstruation revealed that in nineteen of twenty-three cases the graafian follicle had ruptured at the beginning of menstruation, while it was still unruptured in the remainder. These observations, as has been said, were the basis of the theory that ovulation and fertilization precede menstruation.

Although the Reichert theory was accepted by His, it has been firmly and ably opposed by Mall, whose valuable contributions to our knowledge of embryology are so well known. He contends that the application of this

theory to the study of the very early ova which have been reported yields very improbable results as far as the estimation of the ages of these embryos is concerned. On the basis of the Reichert-His theory, for example, the well known Peters ovum, which was obtained thirty days after the last menstruation, is estimated to be only three or four days old. The specimen measured 1.6 x 0.9 mm., and Mall, from a comparison of the rate of growth in lower animals, believes it extremely probable that the Peters ovum was considerably older than four days — probably about fifteen. This view receives support from the fact that Peters' patient had exhibited morning sickness before the missed period.

In a similar way Mall analyzes the reports of other early ova, arriving at the conclusion that most pregnancies take place during the first week after menstruation; and that the duration of the pregnancy is longer if copulation takes place toward the end of the intermenstrual period. And this is explained, if we assume that in the first week, especially the first few days after the cessation of menstruation, the ovum is in the upper end of the tube, awaiting the sperm, and that conception immediately follows copulation. When the fruitful copulation takes place in the latter two weeks of the month, the opposite is usually the case; the sperm wanders to the ovary and there awaits the ovum, and, therefore, on an average, pregnancy is prolonged in this group of cases, when determined from the time of copulation. This explanation fits all the facts, but opposes the Reichert-His theory.

In further support of his opinion Mall cites the figures of Ahlfeld and Issmer, based on a large series of cases. Ahfeld gives the following table of the time of fruitful copulation in relation to menstruation:

	ON LAST DAY OF MENSTRUATION	FIRST TWELVE DAYS AFTER BEGINNING OF MENSTRUATION	FIRST SEVEN DAYS AFTER END OF MENSTRUATION
Married women....	35.55	88.44	88.88
Unmarried women.	25.49	70.98	70.58

The figures of Issmer are as follows:

TIME OF COPULATION	NO. OF CASES	AVERAGE DURATION OF PREGNANCY
First week of menstrual period.	172	277 days
Second " " " "	164	279 days
Third " " " "	72	287 days
Fourth " " " "	45	285 days

The preceding tables indicate that most pregnancies occur during the first week after menstruation.

Finally, attention may be called to the work of Teacher, who made a study of the probable periods of the menstrual cycle at which fertilization and imbedding took place, based on an investigation of twelve selected very early ova, including the famous Teacher-Bryce ovum. The following table shows the results obtained:

FERTILIZATION	DAYS OF MENSTRUAL PERIOD	IMBEDDING
	1	
	2	
	3	
	4	
	5	
Merttens	6	
Rossi Doria	7	
Beneke	8	
	9	
	10	
	11	
	12	
	13	Merttens
Eternod	14	Rossi Doria
	15	Beneke
Peters	16	
Jung	17	
	18	
Von Spee (Glävecke)	19	
	20	
Von Spee (Von Herff)	21	Eternod
	22	
Frassi	23	Peters
Teacher-Bryce and Reichert	24	Jung
Leopold	25	
	26	Von Spee (Glävecke)
	27	
	28	Von Spee (Von Herff)
	DAYS OF SUCCEEDING MENSTRUAL PERIOD	
	1	
	2	Frassi
	3	Teacher-Bryce and Reichert
	4	Leopold
	5	
	6	
	7	
	8	
	9	
	10	

This table shows that, if the ages of the ova be correct, fertilization may occur at any time during the intermenstrual interval, and that imbedding may take place either in the period of quiescence, or in the period when premenstrual or menstrual changes would have been progressing, if pregnancy had not occurred. In other words, Teacher concludes that the menstrual decidua is not to be looked upon as a preparation for the ovum, that menstruation is not an abortion of the unfertilized ovum, and that ovulation does not necessarily coincide with menstruation.

In weighing the evidence above set forth from the embryological point of view, we must bear in mind the important fact that in many of these reports no mention is made of the condition of the ovaries, and that when such mention is made, the presence of a well developed corpus luteum is usually taken as evidence that ovulation has taken place just previously. This view, however, as we have seen (Chapter V), has been disproved by recent histological studies of the life cycle of the corpus luteum, indicating that the fully formed corpus luteum is the product of a progressive developmental change extending over many days, which takes place in the wall of the follicle after the extrusion of the follicles. This fact detracts greatly from the value of such evidence as has been presented in this section.

Histological Studies of Ovary.— Although we are indebted to Fraenkel for the first experimental effort to determine which element in the ovary is responsible for menstruation, and although this author also deduced from his observations the period at which ovulation occurs, it was not until the work of Meyer and Ruge that a method of histological study was resorted to which appears to be free from serious objection. This was not true of the work of Fraenkel, as has already been discussed (Chapters V and VII). The latter author placed the date of ovulation at about the fifteenth to the twentieth days of the menstrual cycle.

The studies of Meyer and Ruge have already been described at some length in Chapters V and VII, as well as the corroborative investigations of Miller and Schröder. It is therefore necessary only to summarize briefly the results of these various authors as they relate to the correlation of menstruation and ovulation.

The plan of study pursued was, in general, a study of the cyclical histological changes in the corpus luteum during the various stages of the menstrual cycle. The latter were determined, not by the uncertain means of the menstrual history, but by a correlative histological study of the endometrium. By this method Meyer and Ruge were able to demonstrate that the life of the corpus luteum, as such, begins at some period between the first and fourteenth days of the menstrual cycle, and that it then passes through a series of cyclical changes which correspond to and produce those noted in the endometrium. In other words, ovulation takes place, according to these observers, either in the postmenstrual or interval periods of the menstrual cycle.

Miller's studies yielded a substantial confirmation of the results arrived

at by Meyer and Ruge, in that ovulation was found to occur in the intermenstrual periods. The exact time was, however, placed somewhat later in the menstrual cycle than by Meyer and Ruge, the process occurring on about the nineteenth day of the cycle, i. e., about nine days before the onset of the succeeding menstrual period.

My own study of five specimens of very early corpora lutea indicates that ovulation occurs practically always in the first half of the intermenstrual period, and probably most frequently between the seventh and fourteenth days. The number of very early corpora lutea reported from all sources, however, is still very small — certainly not over twelve — and hence there is great need of pushing work along this promising line.

Schröder's investigations of this subject are of interest in that he especially has made an effort to correlate the histological findings in the corpus luteum with those in the uterine mucosa. He places the occurrence of ovulation at a period between the fourteenth and sixteenth days of the cycle. The secretory activity of the utricular glands, so characteristic of the premenstrual period, he attributes to the influence of the maturing corpus luteum, while the moderate proliferative changes noted in the glands before the period of ovulation he believes are due to the influence of the ripening graafian follicle before it ruptures.

Summary of Histological Evidence.— This method of investigation appears to be much more reliable than the others which have been discussed. The results of the histological method of study indicate clearly that a very definite relation exists between menstruation and ovulation, but that they do not occur synchronously. Ovulation occurs in the intermenstrual period, its exact date probably varying in different women, but falling usually between the fifth and fourteenth days of the cycle. Menstruation cannot occur without a preceding ovulation, although women often ovulate when not menstruating.

XVI

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CHAPTER XVII

RELATION OF MENSTRUATION TO LACTATION

Is Amenorrhea the Rule During Lactation? — It is a well known fact that in a large proportion of cases menstruation is absent while a woman is nursing her child. Indeed, the absence of menstruation during this time has usually been looked upon as the rule. It is believed by many, however, that in the great majority of cases menstruation reappears before the cessation of lactation. For example, Ehrenfest quotes Czerny and Keller as stating: "We will emphasize the fact, apparently not generally appreciated, that the reappearance of menstruation during lactation is the normal, and that persistent amenorrhea is the exception."

Statistics Bearing on the Discussion.— Ehrenfest found that in a total of 257 lactating women the first menstruation reappeared in 132 instances (51.3 per cent) within twelve weeks post partum. In primiparous women the proportion amounted to 52.3 per cent. Of the total number of cases, it was found that 83.3 per cent menstruated before weaning the child, only 16.6 per cent exhibiting amenorrhea throughout lactation.

Thiemich, on the other hand, from an investigation of some 1200 cases, concluded that menstruation does not appear, so long as the woman suckles the baby and gives no other food whatsoever. When, on the other hand, the woman's breasts are called upon for only a part of the baby's nourishment, menstruation not infrequently reasserts itself.

Essen-Möller states that menstruation reappeared in 60 per cent of 427 women whom he examined during lactation. In about one third the cases it reappeared during the first two months after childbirth. A somewhat similar study by Heil is based on 200 cases. His experience shows that about one half of all nursing women menstruate regularly. He gives a number of reasons which lead him to think that the woman who menstruates during this period represents the normal type.

The statistics of Remfry showed that of 900 nursing women whom he studied 43 per cent menstruated and 57 per cent did not. Brickner found menstruation occurring in 43.3 per cent of 442 nursing mothers; Glass in 40 per cent of 1200 cases; Sundin in from 55 to 59 per cent of 335 nursing women.

Finally, reference may be made to the statistics of Pinard, obtained from the records of 10,886 women who had been confined at the Baudelocque. He says that of women who are nursing for the first time 27 per cent have no menses during lactation; if pregnant for the second time 35 per cent do

not menstruate; if for the third time, 60 per cent do not menstruate, whatever the duration of lactation.

Reasons for the Discrepancy in Statistics.— It will be noted that the figure given by Ehrenfest as representing the frequency with which menstruation occurs at some time during lactation (81.3 per cent) is much higher than the figures given by any of the other authors quoted above. This is explained by Ehrenfest as being due, in part, to the fact that he counts a case as menstruating if the first menstruation appears in less than three weeks after weaning of the infant.

Much more important, to my mind, is the fact that Ehrenfest's figures are based upon a knowledge of the menstrual history throughout the entire course of lactation, the exact date of the first flow and of the cessation of lactation being known. On the other hand, the statistics of most of those who have written on the subject are obtained by questioning nursing women as to the presence or absence of menstruation. Not infrequently menstruation is absent at the time of questioning, but reappears later during lactation. It seems reasonable to believe that figures obtained by such faulty methods of observation can be only approximately correct, and that the actual proportion of lactating women who menstruate is more nearly represented by Ehrenfest's figures.

Cause of Amenorrhea During Lactation.— While we are in the habit of speaking of amenorrhea as a physiological state during lactation, we can only theorize as to the mechanism of its production. In the first place, this question is of course quite separate from the consideration of the cause of lactation. The latter, it may be parenthetically stated, is believed to be due to a hormone originating in the placenta (Halban) or in the ovary (Steinach, Athias). In view of the very great resemblance in the behavior of placental and corpus luteum extracts, Frank very plausibly suggests that the placenta, instead of manufacturing a hormone of its own, acts merely as a reservoir for the corpus luteum substance in the latter half of pregnancy.

In view of our lack of knowledge as to the exact mechanism of menstruation, it seems scarcely profitable to speculate as to the reasons for the frequent absence of the phenomenon during lactation. As we have already seen (Chapter VII), the most recent investigations attribute to the corpus luteum the principal rôle in the causation of the menstrual flow. There is abundant evidence as to the occurrence of ovulation during lactation. Obviously, new corpora lutea are continually being formed in such cases, and yet menstruation does not occur. What new factor it is that counteracts or inhibits the activity of the corpus luteum, if the latter be assumed to cause menstruation, has not been definitely determined. It would certainly seem that the lactating mammary gland is directly or indirectly responsible for this inhibition, most probably through the agency of a hormone. This view, however, is as yet supported by no reliable experimental evidence.

Fraenkel believes that menstruation is absent during lactation, owing to the debilitating influence of the latter upon the woman's organism, and that

when the strength and vitality of the woman reasserts itself, menstruation reappears, even though lactation still be kept up. The evidence in favor of this theory, however, is not by any means convincing.

Ovulation During Lactation.— Numerous clinical reports have been made indicating the possibility of ovulation, as manifested by pregnancy, during lactation. Indeed, the occurrence of pregnancy during the period of lactation is so common that cases of this type are familiar to all practitioners of medicine. The rather striking cases of Roudellet, Joubert, Meigs and Chrobak have already been mentioned in the chapter on "Menstruation and Ovulation."

Fraenkel believed that when impregnation occurs during lactation it is as a rule in women who are amenorrheic, rather than those who have again begun to menstruate. His views, however, are not substantiated by the work of other investigators.

The statistics of Remfry, on the contrary, indicate that the probability of pregnancy is much greater in nursing women who menstruate than in those who do not menstruate. In the former group the chance of pregnancy is placed at 6 in 10, while in the latter class it is only 6 in 100.

In Ehrenfest's series of 209 cases, there were 4 cases of pregnancy in amenorrheic women during lactation, as compared with 22 cases in which the pregnancy followed the first menstruation. This is in accordance with the observation of Heil, who found that pregnancy occurred during amenorrhea in only 29 per cent of women during lactation, the remaining 71 per cent having menstruated one or more times.

It seems fair to conclude that, while a nursing woman may become pregnant either before or after menstruation has reappeared, the occurrence is much more frequent in those women in whom the menstrual function has reëstablished itself.

Influence of Menstruation on Breast Milk.— It cannot be said that opinion is unanimous with regard to the influence of menstruation on the character and amount of the milk secreted by the breasts of the lactating woman. This is a question of some practical importance, for a physician is frequently asked whether breast feeding may safely be kept up during menstruation. At the outset it may be said that this question can practically always be answered in the affirmative. From the observation of a considerable number of such cases, I am convinced that it is rare indeed for menstruation to cause any alteration in the character of the milk, which will work any injury to the child. It is true that occasionally the child will show slight gastric disturbances during this period, and it is perhaps true that in a small proportion of women the systemic influence of the menstrual phenomenon is sufficient to bring about a transient alteration of the milk secretion. Nevertheless, it is a safe rule to assume that there is no risk incident to a continuance of breast feeding during menstruation.

The most recent study of this problem is that of Grulee and Caldwell, These authors cite the work of Vernois and Becquerel in 1853 and that of

Davis in 1856, concluding that little dependence can be placed in their results, owing to faulty methods of study. The one case upon which their own report is based was that of " a baby born with a harelip and cleft palate, nursed for nine months by means of a specially devised breast pump. The mother's menstrual period began six weeks after birth and continued throughout the nursing. The quantity of milk was carefully measured, especially during the last four months of lactation, and there was shown a distinct relation between the quantity of breast milk and the occurrence of the menstrual period. This consisted in a period of increase of breast milk, beginning with the first day of menstruation and lasting from ten days to two weeks thereafter. There then occurred a diminution in the quantity, which reached its lowest point four to seven days previous to menstruation, after which there was a gradual increase."

The objections which at once suggest themselves as invalidating the value of this observation are the possibility of a psychic influence on the mother, and, what is even more important, the fact that the conditions under which the milk was collected were anything but natural. The effort of the authors to minimize the importance of these factors, more especially of the second, is not convincing, and their findings must be looked upon as only suggestive.

As for the effect of menstruation upon the chemical composition of the breast milk, the available reports are practically all of a negative nature. Pfeiffer, Bamberg, Thiemich and Schlicter all find that menstruation causes no changes in the chemical composition of the milk which seem more important than the slight variations seen in all women at various times and as a result of various individual influences.

XVII

LITERATURE

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CHAPTER XVIII

AMENORRHEA

Definition and Varieties.— Amenorrhea is the condition in which menstruation is absent during the reproductive period of the woman's life. Two varieties are usually distinguished, a primary and secondary.

Primary Amenorrhea.— By primary amenorrhea is meant the condition in which menstruation fails to occur at the usual age in girls. In view of the great individual differences in young girls as to the age at which the menstrual function is inaugurated, it is difficult to fix any arbitrary limit beyond which the onset of menstruation may be looked upon as abnormally tardy. Speaking generally, the failure of menstruation to appear before the age of seventeen may be considered to justify the designation of primary amenorrhea.

Secondary Amenorrhea.— Secondary amenorrhea, on the other hand, has reference to the absence of menstruation after the function has already become established. To illustrate, if a woman of thirty, who has always menstruated regularly, misses her period one or more months, she may be said to be suffering with amenorrhea of the secondary variety.

Distinction Between Amenorrhea, Retention of Menses and Suppression of Menses.— These three terms are often confused one with another. Aside from purely academic considerations, it seems to me that a distinction should be drawn between them, if one is to have an intelligent conception of their significance.

In true *amenorrhea,* all the pelvic phenomena characteristic of menstruation are absent. The causative stimulus, whatever it may be, is apparently lacking, so that there is complete absence of the vascular, endometrial and other changes normally associated with menstruation.

On the other hand, all these changes may be present in certain cases in which there is no menstrual discharge whatsoever. Many text books give among the causes of amenorrhea the various forms of mechanical occlusion of the genital canal, which prevent the exit of the menstrual blood. Cases of this type, however, are merely instances of *retention of menses.* Menstruation may occur under these conditions as normally, the only difference being that the menstrual blood can not make its appearance externally.

Of somewhat less importance is the distinction between amenorrhea and *suppression of the menses.* The latter term is, strictly speaking, to be

applied to a suppression or cessation of an individual menstrual period after it has once been inaugurated. To illustrate, if a woman, as a result of getting the feet wet on the first day of menstruation, suddenly ceases to menstruate, she is suffering with suppression of the flow. The severe pain often experienced in this condition emphasizes the difference between it and amenorrhea, in which there is no pain, and usually not even the normal "menstrual molimina."

I am aware that the differentiation made here between these three terms is either not recognized, or at any rate, not emphasized by most authors, but the matter would seem to be of sufficient interest and importance to merit mention.

Classification of Causes of Amenorrhea.— For the sake of convenience, the causes of amenorrhea may be divided into *local* and *general.* The former embrace such conditions as absence or hypoplasia of one or more of the generative organs, or acquired pathological conditions of the pelvic organs. The general causes, on the other hand, have to do with various factors of extragenital nature perhaps involving the organism generally.

The principal groups of causes of amenorrhea may be tabulated as follows:

Local causes:—

1. Congenital absence or malformation of generative organs.
2. Acquired pathological conditions of generative organs.

General causes:—

1. Physiological (puberty, menopause, pregnancy, and lactation).
2. Functional (sudden shock, excitement, chilling or wetting of skin, change of climate).
3. Acute infectious diseases (acute exanthemata, typhoid, pneumonia, malaria, etc.).
4. Constitutional diseases (tuberculosis, chlorosis, diabetes, nephritis, etc.).
5. Mental disturbances, especially insanity.
6. Disorders of the ductless glands.

Local Causes.— Congenital Absence or Malformations of Reproductive Organs.— *Congenital absence of the uterus, of both ovaries, or of both uterus and ovaries,* is of course incompatible with the occurrence of menstruation. In such cases the amenorrhea is of the primary type. A considerable number of such cases have been recorded, absence of the uterus being much more common than absence of the ovaries.

The following personal case illustrates this type of amenorrhea:

L. S., age 20½ years, had never menstruated and had never observed definite menstrual molimina. She was slender but well formed, and not anemic. The breasts were fairly well developed, and there was a normal growth of hair on the mons veneris and in the axillae.

Examination under anesthesia showed the vulva, at first sight, to be

normal. The hymen was of the annular type, and not imperforate, the opening being about 1 cm. in diameter.

Just within this was what seemed at first like a second and imperforate hymen, but which was simply the floor of a shallow fossa less than 1 cm. deep, marking the usual orifice of the vagina. No evidence of the latter could be found. Careful bimanual examination through the rectum failed to disclose any sign of the uterus except an indistinct transverse ridge behind the bladder. The thinness of the abdominal walls and their relaxation by the anesthetic made examination extremely easy. Both ovaries were plainly palpable in their normal positions. The amenorrhea was obviously due to congenital absence of the uterus. This case, together with a second of similar nature, encountered in my own practice, and four others which have been observed in the gynecological clinic of the Johns Hopkins Hospital, were reported by me in a recent paper.

Hypoplasia of the uterus also may be associated with a condition of amenorrhea, as is so frequently noted in women with an infantile type of uterus.

Congenital absence of the fallopian tubes, theoretically at least, might be expected to exert no more influence on the occurrence of menstruation than does the surgical removal of the tubes which is so frequently carried out. It is difficult, therefore, to explain the case reported by Spencer in 1911, in which congenital absence of the tubes was associated with amenorrhea. His patient was a single woman, age 28, who complained of attacks of pain in the right iliac fossa. She had never had any sign of menstruation. The external genitalia and the breasts were normal. The uterus, at operation, was found to be normal, and in place of each cornu there was found a pea-like knob. The ovaries were present, being buried under a layer of peritoneal adhesions. No sign of the fallopian tubes was found.

In spite of the association in this case of amenorrhea with absence of the fallopian tubes, there is no justification for the assumption that they are related as cause and effect. As a matter of fact, all the evidence furnished by modern investigations speaks strongly against any such influence on the part of the tube.

As for congenital absence or atresia of the lower portion of the genital canal (Fig. 28), i. e., the cervix or the vagina, or both, we need only say that such anomalies result in a retention of the menstrual blood above the point of mechanical obstruction. The results of such obstruction to the free exit of the menstrual blood are considered in Chapter XIX.

Acquired Pathological Conditions of Pelvic Organs.— Amenorrhea, or scanty menstruation, as a symptom of local disease in the pelvis, is far less frequent than the opposite condition of excessive menstrual bleeding. The tendency of practically all the usual forms of pelvic disease, such as the inflammatory conditions and the neoplasms, is to produce menorrhagia rather than deficient menstruation. Occasionally, however, the

pathological lesions are of such a form as to involve serious impairment of the endometrium or of the secreting structure of both ovaries. In either case the result may be cessation of menstruation.

Atrophy of the endometrium, with resulting amenorrhea, is especially apt to occur in connection with grave puerperal infections. Occasionally even gangrene of the endometrium occurs under such conditions, the sloughing endomentrium being cast off from the uterus with resulting scar formation. In most cases of puerperal infection of such virulent type, the patient succumbs. If she recovers, menstruation frequently fails to reappear. Similar atrophic changes in the endometrium are occasionally noted after acute and virulent gonorrheal infections, as well as in association with the acute exanthematous diseases, such as scarlet fever. When such atrophic or destructive lesions occur in the lower part of the genital canal, the result is frequently gynatresia, with retention of the menses.

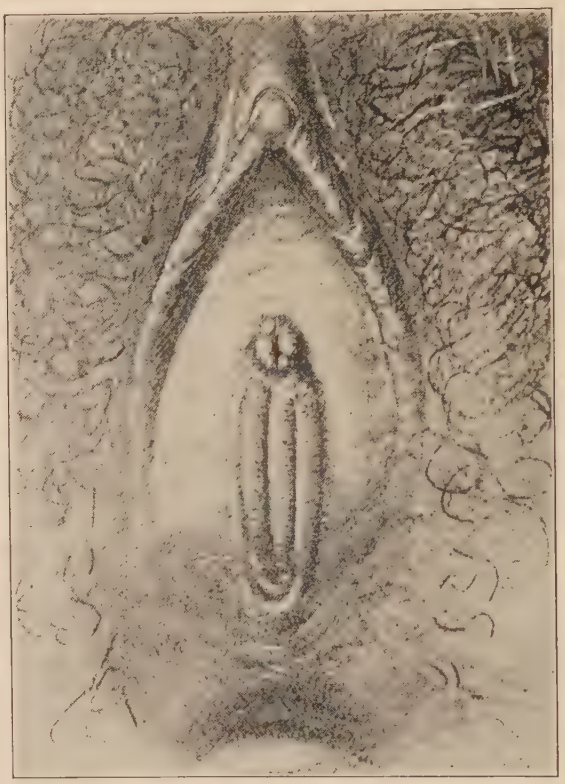

Fig. 28.— Entire Absence of the Vagina, With Indication of Double Hymen.

The external genitals are normal (Kelly).

As far as the ovaries are concerned, the only type of anatomic alteration capable of inducing amenorrhea is one which involves a *destruction or loss of function of all secreting ovarian tissue.* Such a sequel, while not very common, is observed more frequently in connection with neoplasms than with inflammatory diseases. In a recent case of my own, the condition found at operation was one of bilateral dermoid cysts of the ovaries. Each cyst was about the size of an orange and had apparently destroyed the entire cortex of the ovary. The woman, who was thirty-four years old, had not menstruated for eight months.

General Causes.— *Physiological Amenorrhea.*— In a large proportion of cases amenorrhea is noted one or more times during the "dodging" periods of *puberty* and the *menopause.* The proportion of girls who menstruate regularly from the very inauguration of the function is stated by

Emmett to be as high as 72.33 per cent, but my own impression is that this estimate is too high. It is extremely common for girls to skip one or more periods from time to time during the first year or two of menstrual life. The same thing is true of the other end of the reproductive life, the menopause, for the complete cessation of the menstrual function is often preceded by periods of amenorrhea of varying length.

Amenorrhea is the rule during *pregnancy*, although menstruation may occur occasionally during the first month or two of gestation. Rarely the periods recur for a longer time, cases being recorded where menstruation has continued up to the seventh month of pregnancy.

As regards *lactation*, the statement has usually been made that amenorrhea is the rule, though exceptions are frequent. As a matter of fact, if the history be followed throughout lactation, i. e., from parturition to the weaning of the child, it will be found that in the majority of cases menstruation returns at some time before the end of lactation. The proportion of cases in which menstruation occurs during lactation is placed by Ehrenfest as high as 81.3 per cent.

For a further discussion of these subjects the reader is referred to Chapters IX, XIII and XVII.

Functional Amenorrhea.— This term is not altogether satisfactory, inasmuch as many of the other causes herein given for amenorrhea are also, in the final analysis, due to functional derangements of the ovary. No other term, however, suggests itself for certain cases of amenorrhea which occur in the absence of any recognizable disease, either local or general. To this group belong the cases in which *chilling of the body* or *wetting of the feet* or hands inhibits the appearance of menstruation; or else, if it has already begun, brings about sudden checking of the flow. Cases of the latter type are better spoken of as suppression of menses, as already suggested.

The same inhibitory influence may be exerted by *psychic and emotional disturbances*. The best illustration of the power of the mind over the menstrual function is furnished by the frequent occurrence of amenorrhea in women who have an intense longing for pregnancy, or, on the other hand, in unmarried women who fear that they may be pregnant. Suppression of the menses also is the occasional result of sudden fright, grief, joy or other emotional disturbances in the menstruating woman. Many cases of amenorrhea were observed among German and Austrian women during the recent war *(kriegsamenorrhöe)*.

Another common cause of functional amenorrhea is *change of climate*. This fact has been known for a long time, but even now comparatively little of a definite nature can be stated as to the exact reason for this phenomenon. I have had an opportunity of observing it in many immigrants from Europe and can testify to its great frequency. In discussing the comparative physiology of menstruation we laid great stress upon the fact that the function is greatly influenced by climatic and environmental

conditions. (Chapter II). We also presented evidence in favor of the view that the polyestrous sexual season of the human female probably represents an evolution from a primitive non-estrous cycle. The interesting suggestion has been made that the amenorrhea so frequently seen after change of climate perhaps represents a tendency towards reversion to the primitive monestrous type.

Finally, this form of amenorrhea is often observed as a result of any condition which brings about a *deterioration in the general health* of the girl or woman. Such factors as unhygienic surroundings and overwork are of great importance. Not only the amount of work, but also its character, may be very harmful, as in the case of girls who are employed in tobacco factories, tailor shops, department stores, etc. Not only physical overwork, but also mental overtaxation, is apt to be associated with amenorrhea, so that it is therefore frequently noted in the growing girl who is being overburdened with school work.

Amenorrhea Due to Acute Infectious Diseases.— In a general way it may be said that the influence of the various acute infectious diseases upon menstruation is proportionate to the severity of the individual case. Mild cases of typhoid, pneumonia, or other diseases of this type sometimes exert very little influence on the course of menstruation.

In other cases, again, and almost always when the malady is clinically very severe, a powerful inhibitory effect is exerted upon menstruation. This is especially true of typhoid, during which disease, according to Osler and McCrae, amenorrhea is the rule. The shorter course of pneumonia makes the inhibitory effect less conspicuous, although even here menstruation is often skipped. Occasionally, it is true, menstruation appears to be increased in amount by various infectious diseases, as in certain cases of influenza (Haken). Such an effect, however, is certainly less common with infectious diseases than the occurrence of amenorrhea. For a further discussion of this subject see Chapter XXV.

Amenorrhea Due to Constitutional Diseases.— Among the constitutional disorders which are capable of producing amenorrhea may be mentioned chlorosis, tuberculosis, diabetes, nephritis, syphilis, alcoholism, drug addictions, etc. While this subject is more elaborately discussed in Chapter XXV, mention may here be made of a few facts bearing on this relationship.

Chlorosis.— This disease, as is well known, is especially apt to develop in young girls at or about the time of puberty. This fact, together with the fact that it is, according to most authors, not observed in males, is responsible for the tendency to associate its causation with a hypoplasia of the reproductive apparatus. In spite of the classic work of Virchow, there is no indisputable evidence to justify this belief. The principal gynecological symptom of "green sickness," as chlorosis is often called, is scanty menstruation or complete amenorrhea. Absence of the menses is extremely common, Cabot finding it in 120 of a series of 387 cases.

Tuberculosis.— The relation of tuberculosis and menstruation is of the

greatest importance, as will be emphasized elsewhere (Chapter XXV). For the present we may say that amenorrhea is usual in advanced cases of phthisis, and, what is even more important, that it is frequently a symptom of incipient tuberculosis. In searching for the cause of amenorrhea in young women, one must always bear in mind the possibility of an early tuberculous process in the lungs.

Other constitutional disorders.— In diabetes and nephritis, amenorrhea is a frequent concomitant. The relationship is apparently not at all a direct one, the amenorrhea merely reflecting the general lowering of vitality so characteristic of aggravated forms of these diseases. In syphilis also, it sometimes happens that menstruation is absent, as in the three cases reported by Meirowsky and Frankenstein. Other constitutional conditions in which amenorrhea may be observed are lead poisoning, alcoholism, and morphinism.

Influence of heredity.— Under this head, it may be of interest also to note that in certain cases the factor of heredity has been credited with an influence in the existence of amenorrhea. A rather striking case of this type is reported by Hoover and Marden. Their patient was a Greek woman of forty who had never menstruated. She was in good physical condition, of average size and development, and rather intelligent. She had been married at the age of 15 and had had 11 children. The youngest of these was four years old. Her grandmother had never menstruated, and her mother had menstruated only once or twice every one or two years. The 14 year old girl of the patient had not yet menstruated. She herself had never observed any molimina, having always "lived like a man."

Amenorrhea Due to Mental and Nervous Disorders.— In practically all forms of insanity, amenorrhea is exceedingly common. This is especially true of the depressive forms of insanity, such as melancholia. When menstruation is present, it is apt to be scantier than normal, and to exert an unfavorable influence on the mental malady. The same facts may be stated with regard to the allied mental conditions associated with drug addiction, especially morphinism.

Amenorrhea Due to Disorders of the Ductless Glands.— It is now universally accepted that the ovary is an internal secretory organ, and that it is intimately bound up with all of the so-called ductless glands. It is therefore almost a truism to say that menstruation is influenced by derangements in practically any part of the ductless gland chain. Aside from the ovary itself, amenorrhea is most likely to be associated with secretory derangements of two of the ductless glands, viz., the thyroid and the pituitary.

Thyroid.— There is considerable difference of opinion as to the influence of thyroid diseases upon the menstrual function. In some cases of hyperthyroidism, it is apparently unaltered, in others it seems to be decreased, and in still others it appears to be increased. The same statements may be made with regard to the opposite condition of hypothyroidism. This apparent paradox is not difficult to comprehend when one bears in mind the pluriglandular nature of most ductless gland disorders. Speaking gener-

ally, it may perhaps be said that amenorrhea, with which we are concerned in this chapter, is more frequent in hyperthyroidism than in hypothyroidism, bearing in mind that there are many exceptions to this general rule.

Pituitary.— The *adiposogenital dystrophy of Fröhlich.* The form of pituitary derangement which is most frequently associated with amenorrhea is that which is due to hypopituitarism, and which is clinically associated with obesity.

Among the causes of amenorrhea given by almost all text books on gynecology is adiposity. The relation which exists between obesity and absence of the menstrual flow is an interesting one, and has been the subject of much discussion, especially within recent years. Formerly it was believed by some that the obesity in these cases was the cause of the amenorrhea, while the exact reverse was held by others. Within recent years, however, an entirely new light has been thrown upon this relationship by the interesting work of Paulesco, Cushing, Fröhlich, and others, upon the pituitary body. It has been found that in certain cases of disease of this body there is produced an interesting grouping of symptoms, the most conspicuous of which are obesity and sexual hypoplasia. In women the physiological manifestation of this hypoplasia is amenorrhea.

It was furthermore shown that this same syndrome — *the adiposogenital syndrome of Fröhlich* — could be produced experimentally in animals by partial removal of the hypophysis. Many such experiments are reported by Cushing and others. Since disturbance of the pituitary can thus be shown to be capable of producing amenorrhea and obesity, it seems reasonable to assume that both these symptoms, when associated clinically, are produced by the same underlying cause, and that this cause is probably to be sought in some disturbance, functional or otherwise, in the pituitary body. For a further discussion of this subject, see Chapter XXIV.

Significance of Amenorrhea as a Symptom.— From the above discussion of the etiology of amenorrhea, it appears that it must be regarded as only a symptom of any one of a large number of underlying causes. In spite of the fact that it is only a symptom, it is often in itself a source of grave concern to the patient. A very prevalent belief among the laity is that absence of menstruation will lead to consumption — that the patient will "go into decline." Every practicing physician encounters this notion time and time again.

This idea is greatly strengthened, in the minds of the laity, by the fact that many amenorrheic patients are anemic, and that they frequently suffer with functional disorders of the heart and stomach. Furthermore, it is true that menstruation usually ceases in the late stages of tuberculosis. The inference is thus drawn that amenorrhea stands in some specific relationship to consumption. While this is incorrect, it must not be forgotten that in certain cases of tuberculosis, especially in young women, amenorrhea is a very early symptom.

Is Amenorrhea Detrimental to Health? — The question is frequently

asked as to whether the existence of amenorrhea is in any way detrimental to the general health. From what has already been said it will seem that, if anything, its influence is apparently in some cases conservative, as when it occurs in conditions of lowered vitality. When its causation is more obscure, and especially when the general health of the patient does not seem to be deteriorated, no such protective influence can be assumed. There is no evidence, however, to show that the non-occurrence of menstruation in such cases is in itself detrimental to the health of the woman.

The old theory that menstruation is a cleansing process, ridding the body of poisonous and obnoxious materials, has led some to believe that amenorrhea allows a retention of such products, and that it is therefore injurious to the woman's health. In other words, it is believed by some that amenorrhea may cause a "menorrhemia" analogous to the uremia which follows anuria. As already stated, however, no scientific evidence has been adduced in support of such a belief, and, indeed, clinical evidence is quite opposed to it.

Symptoms Which May Be Associated with Amenorrhea.— In certain cases, absence of menstruation is associated with mild neuroses or psychoses, and occasionally with a condition of melancholia. In such cases, however, it seems highly probable that these manifestations are due to worry and anxiety over the non-appearance of the menses rather than to any direct effect of the amenorrhea itself.

In some patients headache is complained of, this being usually much accentuated at the time of the menstrual periods. Asthma has been described as occurring in some cases of amenorrhea, but I have never observed such a case. In rare cases more serious symptoms may be noted, although it is a question as to how far these may be directly attributed to the amenorrhea. Gemmell, for example, cites the case of a girl of sixteen whose menses were normal up to the time she went to boarding school, when they ceased. In about one month she suddenly became blind in one eye. At the end of three months she was practically blind in both. This blindness was caused by hemorrhages into the vitreous. After this she received treatment to bring on her periods, and at the time of the report had regained the sight of one eye. The presence of the hemorrhages would seem to eliminate the possibility of the blindness being hysterical in origin. It is a question, however, whether these hemorrhages are not to be looked upon as representing a vicarious menstruation, in which case the resulting blindness could scarcely be attributed to the amenorrhea in itself, except in so far as this was responsible for the vicarious phenomenon.

Rosenberger speaks of the occurrence of optic nerve atrophy and other ocular conditions in amenorrhea, explaining them as due to pressure on the optic chiasm by an enlarged anterior lobe of the pituitary body. He suggests syphilis as a possible cause. Such occurrences, however, must be exceedingly rare.

In some cases of amenorrhea the normal discharge of menstrual blood is

replaced by a white mucous discharge, the menstrual leucorrhea or "fluor albus." In other instances, again, the patient retains a "menstrual memory," so that even though the menses are absent there is a certain amount of local or general disturbance at the time of the menstrual periods. Finally, in perhaps the majority of cases, the woman experiences no subjective signs whatsoever of the menstrual period.

When the menses are absent as a result of mechanical occlusion of the genital canal, on the other hand, menstrual molimina are perceived by the patient each month. This is only what might be expected, inasmuch as the menstrual blood is given off by the endometrium regularly. The gradual accumulation of the menstrual discharge behind the point of obstruction results sooner or later in the formation of a tumor mass, which is productive of further pressure symptoms (see Chapter XIX).

The suppression of menses which is so often brought about by wetting of the feet or chilling of the body after the menstrual congestion has already set in is also not infrequently associated with local and even general discomfort. Heaviness and bearing down in the pelvis are often complained of, and sometimes a slight febrile reaction is observed, together with headache and malaise.

In amenorrhea associated with diseases of various kinds there are no symptoms referable to the amenorrhea itself, the clinical picture pertaining altogether to the underlying disease.

In cases of more obscure causation, such as those due to change of climate, or to disturbances in the ductless gland system, the occurrence of the amenorrhea appears to entail no symptoms, other than such nervous or mental symptoms as are to be explained by worry over the failure of the menses to appear. The same innocuousness is characteristic of the physiological amenorrhea of puberty, the menopause, pregnancy and lactation.

Diagnosis of Cause.— As far as the mere existence of amenorrhea is concerned, no diagnostic problem is presented. The aim in all cases of amenorrhea, however, should be to determine the cause of the condition. In some cases this will be very easy, in others difficult or perhaps impossible.

The diagnosis of retention of menses due to mechanical obstruction of the genital canal, either congenital or acquired, can usually be made without difficulty by examination of the reproductive organs. While such an examination should always be avoided in the case of young unmarried women, it is indicated in cases of primary amenorrhea, with well marked menstrual molimina or other symptoms which suggest gynatresia. The examination should preferably be made under anesthesia.

The diagnostic problem presented by cases of physiological amenorrhea is often anything but simple, owing to the frequent difficulty of distinguishing between the simple amenorrhea of puberty or the menopause on the one hand, and the amenorrhea of pregnancy on the other hand. Especially at or near the age of the menopause is this problem apt to arise. It is sometimes rendered difficult by the adiposity often accompanying the climacteric

and by the fact that subjective symptoms of pregnancy are apt to coexist, thus bringing about a striking mimicry of pregnancy (pseudocyesis). Even with the most careful examination, it is not always possible to make a positive diagnosis at the first examination.

With regard to amenorrhea due to disorders of the ductless glands, it is possible, in a certain number of cases, to fix upon such a causation from the existence of definite symptoms of disturbed function in the thyroid, pituitary, or other internal secretory glands. The most clear cut cases of this group are those of the tpye of adiposogenital dystrophy. A presumptive diagnosis of the latter may be made when absence of the menses is associated with rather sudden and perhaps very great increase in weight, without any other apparent cause. Occasionally, of course, conditions may be present which make it possible to arrive at a positive diagnosis, as in the case of pituitary or suprarenal tumors. Unfortunately, however, it is difficult in many instances to make more than a presumptive diagnosis.

A word of caution must be uttered against deciding too quickly that a case of amenorrhea is due to ductless gland derangement, when perhaps a more thorough examination would reveal some much more tangible cause for the condition, such, for example, as incipient tuberculosis.

Treatment of Amenorrhea.— Physiological amenorrhea, of course, requires no treatment. The treatment of pathological amenorrhea may be considered under the following heads: (1) treatment of the underlying cause; (2) general treatment; (3) medicinal treatment; (4) organotherapy.

Treatment of Underlying Cause.— It goes almost without saying that whenever it is possible to remove the cause of amenorrhea, this is the fundamental step in the treatment. When, for example, the menses do not appear because of an obstruction in the genital canal, the indication is to relieve the obstruction (see Chapter XIX). Again, when amenorrhea is merely an incident in the course of some disease, either acute or chronic, no treatment directed to the relief of the amenorrhea itself is indicated. In other words, since amenorrhea is usually a symptom of some underlying pathological state, an effort should always be made to discover the causative condition and treat it. What we shall have to say in the following paragraphs has to deal largely with those very numerous cases in which the cause is not definitely ascertainable or in which no specific treatment seems possible.

General Measures.— In all cases of amenorrhea it is extremely important to impress upon the patient the necessity of a proper hygienic régime. *Open air recreation,* such as that afforded by walking, riding, boating, etc., is of great importance when there exist no contra-indications. It is scarcely necessary to say that such active forms of exercise would be, to say the least, very inadvisable in the amenorrhea of early phthisis. In the latter form of the disorder the need of fresh air, combined with rest, is of the greatest importance. The *diet* should be of nutritious and easily digestible food stuffs, including a goodly portion of fruits and vegetables,

practically all of which are rather rich in iron. Constipation should be relieved when present, preferably by some one of the vegetable purgatives.

Much stress must be laid upon the importance of *avoiding overwork,* either physical or mental. Such sociological aspects of the problem are not always easy to correct, but they are of great importance. Mental fatigue, such as is seen in so many girls in our modern schools and colleges, is perhaps even more important in the causation of amenorrhea than is physical overwork.

Among other general measures which are often of value in the treatment of amenorrhea may be mentioned *hot baths* and *hot drinks.* This is especially true in the sudden suppression of the menses which follows wetting of the feet or chilling of the body. In some of these cases the flow may be reëstablished, although more frequently it remains absent until the time of the next period.

Medicinal Treatment.— In certain forms of amenorrhea treatment by drugs is of very great value, in others it is useless. The two classes of drugs which are most extensively utilized in the treatment of amenorrhea are the *hematinics* and the *emmenagogues.* The former answer a real indication in many cases of amenorrhea and it is therefore not surprising that they yield successful results far more frequently than do the emmenagogues.

The most important indication for the administration of hematinics in amenorrhea is, of course, in those cases which are clearly secondary to chlorosis and other forms of anemia.

Iron in the Treatment of Amenorrhea.—No drug can fully take the place of iron in the treatment of the latter group of cases. It may be administered in various forms, and in combination with other hematinics or general tonics. Perhaps the most popular method of giving iron is in the form of the well-known *Blaud's pill* (pil. ferri carbonat.), which may be prescribed in doses of one or two pills after each meal. The dried sulphate of iron is also frequently employed, in doses of one or two grains three times a day. Where there is a tendency toward constipation, as there is so apt to be during the course of medication by iron, it is often advisable to combine the iron with aloes or nux vomica. Arsenic also may be administered together with the iron. I have personally often made use of the following prescription:

Ferri exsiccati .....gr. xlv
Arseni trioxid .....gr. ¾
Strychnin. sulphat. .....gr. ss.
M et div. in caps. no. xxx.
Sig. One capsule after each meal.

Another convenient and effective, though less agreeable, method of administering iron is in the form of the *tincture of chlorid* (tinct. ferri chlorid.). This may be given in increasing doses, beginning with seven or eight minims well diluted, and taken through a glass tube. The dose may

gradually be increased up to twenty or even thirty minims. In connection with this preparation, it is worth remembering that, like wine, it improves with age, so that the best results are not to be obtained with very fresh preparations.

The *syrup of the iodid of iron* (syr. ferri iodid.) is also frequently employed, especially in girls at or near the age of puberty. It may be given in doses of from twenty to thirty minims three times a day. The citrate, the phosphate, and the tartrate have all been employed by various clinicians. Herman recommends the following formula:

Ferri et ammon. citrat..... ʒ i
Potass carb. .....gr. xxiv
Spir. chloroform ..... ʒ i
Aq. dest. q.s.ad..... ℥ vi
M
Sig. One dessertspoonful after each meal.

In addition to the various preparations of iron already mentioned, all of which are official, attention may be called to the fact that the National Formulary offers a number of preparations, chiefly elixirs, for the convenient and agreeable administration of iron. Among them I may mention the following, the average dose of all being one dram: Elixir ferri hypophosphitis, elixir ferri lactatis, elixir ferri phosphatis, the well-known elixir ferri, quininae et strychniae, syrup. ferri hypophosphitis and syrup. lactophosphatis. Mention may also be made of tinct. ferri citrochlorid, the average dose of which is ten minims, and of the pil. ferri compositae.

No matter what form of iron is resorted to in the treatment of amenorrhea, its use should be kept up for a long time, rarely less than three months, and often much longer. Failure to restore the menstrual function in cases of chlorosis is usually due either to insufficient dosage or to too early cessation of the treatment.

Arsenic.— Next to iron, the most valuable of the hematinic drugs is arsenic. In my experience, however, it is distinctly inferior to iron in the treatment of the amenorrhea of chlorosis. When the anemia is not of the chlorotic type, arsenic is often a very valuable drug. It is usually administered in the form of *Fowler's solution* (liq. potassii arsenit.) in gradually increasing doses, beginning with three minims well diluted in water three times a day, and increasing by the addition of one minim to the dose every second or third day until the point of physiological saturation is reached. This, as is well known, usually makes itself evident by supraorbital neuralgia, watering of the eyes and nose, puffiness of the eyelids, or gastro-intestinal irritation.

Questionable Value of Emmenagogues.— The use of emmenagogues in the treatment of amenorrhea can scarcely be looked upon as a rational therapeutic measure, although it is practiced quite generally. I confess to

an extreme skepticism concerning the results of such medication. Among the laity, especially, there is a widespread belief that it is a simple matter for the physician to prescribe medicines to "bring on" the menstrual flow. Bearing in mind the varied and often obscure etiology of amenorrhea, and the fact that in many instances it appears to be a somewhat protective phenomenon, the fallacy of such a notion is obvious.

Some one has compared the menstrual mechanism to the works of a clock, remarking that "if the works are in good order, the clock will strike regularly." With amenorrhea, therefore, the indication is clearly to put the entire menstrual mechanism in good order rather than to attempt by means of emmenagogues to correct a condition which, to say the least, may be perfectly harmless. In view of these personal convictions, I shall do little more than mention a few of the drugs which have been credited with more or less powerful emmenagogue properties.

Perhaps the best known of these is *manganese,* which is employed either in the form of the dioxid (mangani dioxidum) or of the permanganate of potash (potassii permanganat). Many prefer the former, which is given in doses of from two to five grains, while the permanganate is given in smaller doses, one half to two grains.

The following prescription, which would seem to combine the good effects of iron, arsenic, and manganese, has been recommended by Kelly:

Ferri sulphat. .....gr. ii
Acidi arsenos. .....gr. 1/40
Mangani dioxid. .....gr. iii
M. et ft. pil. Mitte tales 100.
Sig. One pill three times a day.

Another drug, which was first used by the French, and which has enjoyed a wide vogue as an emmenagogue, is *apiol* (oil of parsley), which is administered in capsule in doses of from three to ten minims after each meal. Its administration should be begun several days before the usual time for menstruation.

An emmenagogue effect is also ascribed to many of the vegetable purgatives, and especially to *aloes.* This drug has in the past been widely used for this purpose. Marshall Hall speaks of it as being just as certain in many cases as quinin is in the treatment of malaria. It is frequently combined with iron and perhaps nux vomica, as mentioned above. The official pill of aloes and iron (pilul. aloes et ferri) is also not infrequently used, in doses of from one to four pills. The following pill, containing aloes, was recommended by Goodell:

Extracti aloes ..... ʒ i
Ferri sulphatis exsiccati..... ʒ ii
Asafetidae..... ʒ iv
Fiant pilulae no. c.
Sig. From one to three pills three times a day at each period.

There is little doubt that aloes causes pelvic hyperemia, but whether it has any directly emmenagogue effect is open to question.

Mention may also be made of asafetida, guaiacum, borax, cantharides, and all the ecbolics, especially ergot and quinin. The use of fuchsin has been recommended by Mondy, who reports a case of amenorrhea of four years standing successfully treated by this drug given in pill form three times a day.

The following drugs have also been used in the treatment of amenorrhea, although their effect is very uncertain: Santonin (gr. ii or gr. iii t.i.d.); oleum sabinae (m iii to m v t.i.d.); oleum rutae (m iii to m v t.i.d.); oleum tanaceti (m iii to m v t.i.d.); tinctura cantharidis (m xx to m xxx t.i.d.); tinctura hellebori nigri (m xx to m xl t.i.d.). For reasons which have already been discussed, my own feeling is that it is not good therapeutics to try to "bring on the flow" with such drugs.

Organotherapy of Amenorrhea.—A discussion of this subject will be found in Chapter XXVI.

XVIII

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CHAPTER XIX

GYNATRESIA AND RETENTION OF THE MENSTRUAL DISCHARGE

General Conditions.— By gynatresia is meant a closure of some portion of the genital tract. In by far the largest number of cases the atresia is noted in the lower portion of the vaginal canal. While the condition often causes no symptoms before puberty, it may be of serious import when menstruation has been inaugurated. The immediate effect of gynatresia in cases of the latter type is to cause a retention of the menstrual flow. Clinically, the condition is commonly considered to be amenorrhea, although as a matter of fact menstruation really goes on approximately as in the normal woman, with the exception that the menstrual discharge is prevented by the obstruction from reaching the exterior (Chapter XVIII).

Types of Gynatresia.— Two general types of this condition may be described, the congenital and the acquired. Since there are now many who believe that even the so-called congenital cases are really due to infection and inflammation, it has been proposed that the terms primary and secondary be applied to the two groups (Brothers).

Causes of Primary or Congenital Gynatresia.— The former view was that practically all the so-called congenital cases are due to a defect of development in some portion of the müllerian ducts. According to Dohrn, these ducts unite at about the seventh week of embryonal life, while by the end of the third month the differentiation into uterus and vagina is already evident (Kussmaul). The hymen, it may be added, does not appear until about the nineteenth week. The genital canal is thus, under normal circumstances, completely developed at about the fifth month.

Gynatresia may occur when the müllerian ducts have fully united or when they have remained separate throughout a greater or less extent of their course. Of 145 cases of primary menstrual retention collected by Brothers, there was a single genital canal in 80, as compared with 60, in which the canal was double. Practically any of the well known forms of malformed uterus may be associated with gynatresia, such as uterus didelphys, uterus bicornis or unicornis, uterus biseptatus, etc. The vagina may be single or double.

The Nagel-Veit Theory.— As already intimated, the theory that many of the obstructions which may occur in the vaginal canal are congenital has been vigorously disputed. Nagel believes that they are all acquired. Furthermore, he does not believe that congenital absence of the vagina can be associated with normal development of the uterus, tubes, and ovaries, and

he asserts that when the vagina is atretic in otherwise normal cases, the defect is due to adhesion of opposing vaginal surfaces as a result of loss of the epithelial covering. These changes may occur as a result of inflammations in very early life, or even before birth.

Veit not only supports Nagel's views as to the acquired nature of these abnormalities, but goes a step further. He believes that when a hematosalpinx is present with gynatresia, the evidence is complete that there exists some infection of the genital tract, and that the condition is acquired and not congenital. It is the infection present in these cases which causes an inflammatory closure of the abdominal end of the tube, thus permitting the development of the hematosalpinx.

Imperforate Hymen.— The most common congenital obstruction is usually looked upon as an imperforate hymen, although the studies of Bell indicate that the obstructing membrane in this group of cases is not the hymen, but an "imperforation" of the lower end of the vagina. Bell credits Matthews Duncan with having first called attention to this fact. Histological study of the membrane in these cases shows that, while the outer surface is covered with stratified squamous epithelium, similar to that of the vulva, the inner surface is often covered with columnar epithelium. This, in Bell's opinion, proves that the membrane cannot be the hymen, for the latter is covered on both surfaces by stratified squamous epithelium.

If the Nagel-Veit theory be correct, the origin of these cases is to be sought in an acquired factor of one form or another, although they have in the past been quite generally looked upon as congenital. That at least some of them are of acquired origin admits of no doubt. Veit, for example, reported a case of complete atresia of the hymen in a woman who was pregnant at term, and also a case in which the woman had previously menstruated regularly, over a period of several years. Obstruction by an imperforate hymen results first in distention of the vagina with blood (hematocolpos). This is followed in turn by distention of the cervix (hematotrachelos), then of the uterus (hematometra), and finally of the tubes (hematosalpinx). (Fig. 29.)

Other Forms of Obstruction.— Much less frequently the obstructing membrane may be located higher in the vagina, or perhaps in the cervix. Complete absence of the vagina, of congenital origin, cannot, according to Nagel, exist with normal pelvic organs, and cannot therefore be a cause of hematometra. This view would seem to be corroborated by the findings in six cases of congenital absence of the vagina which I recently reported. In all of them the uterus was absent.

Secondary or Acquired Gynatresia.— In the majority of cases secondary gynatresia is due to an inflammatory or ulcerative process which results in adhesions between the vaginal walls. The more important causes may be briefly set down as follows:

Puerperal Infection or Lacerations.— Occasionally, as a result of puerperal infection, there may be more or less severe sloughing of either

the cervical or vaginal mucosa, with cicatricial closure of the canal as a result. Less frequently extensive lacerations may produce the same effect.

Infectious Diseases.— The acute exanthemata may rarely cause severe ulcerative inflammation of the vagina, with resulting gynatresia. Scarlet fever and diphtheria are perhaps of greatest importance in this respect. In addition to the general infections, intense local infections with the gonococcus may at times be followed by gynatresia.

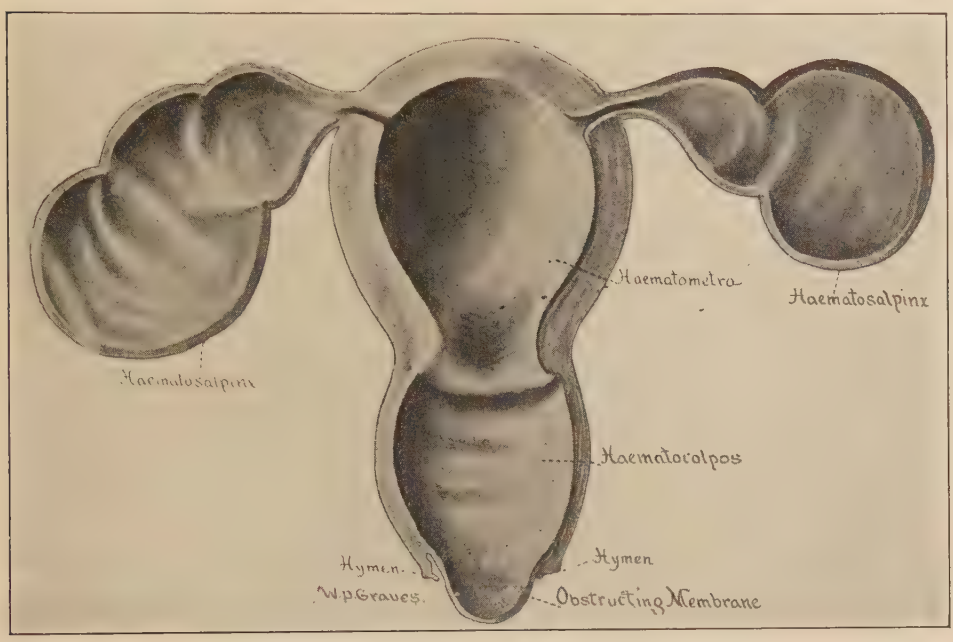

Fig. 29.— Acquired Atresia of the Vagina or Hymen.

A semidiagram, showing the cavities formed in the genital tract by the obstructed menstrual blood. Hematocolpos in the vagina, hematometra in the body of the uterus, and hematosalpinx in the tubes (Graves).

Trauma.— Various forms of external injury may be followed by closure of the vaginal canal. Such injuries as those produced in children by falls astride a chair are especially important in this connection. Under this same heading may be placed the injuries caused by corrosive substances, such as acids. In the cervix the most frequent cause of atresia of this type is excessive cauterization, either with chemicals (zinc chlorid, carbolic acid, etc.) or with the actual cautery. Spalding has recently reported a case of cervical occlusion, with retained menses, observed in a woman of 29, as a result of an improperly performed amputation of the cervix. The uterus was distended to the size of a grapefruit.

Senile Atresia.— Special mention may be made of this cause of gynatresia, on account of its frequency and consequent importance. As a woman approaches the menopause, even before menstruation ceases, retrogressive

changes in the mucosa of the genital canal may become marked (see Chapter XIII). The thin, pasty, anemic appearance of the vulvar and vaginal mucosa in women at this period is due to a gradual replacement of the lining epithelium with connective tissue. This retrogressing mucosa is exceedingly liable to inflammatory processes (senile vulvovaginitis), with a marked tendency to ulceration. The sequel to the latter is often a pronounced contraction and perhaps even complete closure of the vagina. The same process may less frequently involve the cervix or the body of the uterus.

When atresia of this type occurs in the woman in whom menstruation has not yet ceased, the result is of course retention of the menstrual discharge.

Even in women far beyond the age of the menopause, however, gynatresia may be associated with extensive accumulations of blood in the generative canal. A good illustration of this fact is furnished by the recent case of Gellhorn. His patient was a woman of 74, who had passed the menopause 35 years previously. An attack of severe pain led to the discovery of a "large fluctuating tumor which filled the entire pelvis and extended upward almost to the umbilicus." Examination showed that there was senile atresia of the vagina, the canal being closed. At operation the tumor was found to consist of a large hematocolpos, hematometra, and double hematosalpinx. Panhysterectomy was followed by death from embolism on the fifteenth day. Examination of the specimen showed that the source of the blood in this case was an adenocarcinoma of the fundus. A somewhat similar case has been reported by Sondheimer. Other instances of postclimacteric hematometra are recorded by Chrobak, Savidge, Stein, Verdier and others.

Mechanical Occlusion from Within or Without the Genital Canal.— Perhaps the most familiar type of mechanical occlusion of the genital canal is that occasionally produced by carcinoma of the cervix. It is not rare for cervical cancer, especially adenocarcinoma, to block the canal completely, so that the menstrual blood is backed up in the uterus (hematometra). As a rule, however, secondary infection soon takes place, pyometra being the result. Other tumors, such as polypi, may occasionally cause similar occlusion of the genital canal.

Another relatively frequent form of genital occlusion, with accumulation of blood, is found in the tube as a result of torsion, usually in connection with torsion of the pedicle of an ovarian tumor. It must be borne in mind, however, that the bloody content of the tube in these cases is not retained menstrual blood, but a hemorrhagic exudate due to the disturbance of the tubal circulation.

A rather interesting case has been reported by Child, in which he attributes "regurgitant menstruation through the fallopian tubes" to an "antipregnancy button" which had been worn by the patient for three months without removal. In addition to the difficulty of excluding tubal pregnancy in such a case, however, there is also the possibility of the bloody exudate in the tubes having been due to tubal infection, perhaps consequent to the presence of the foreign body.

Symptoms of Gynatresia.— Until the inauguration of the menstrual function, gynatresia produces no symptoms, and hence is commonly unrecognized. Often attention is directed to the condition by the failure of the menses to appear at the usual age. As a rule, however, there is a history of menstrual molimina in such cases. Even though there is no external appearance of the menses, the girl suffers more or less discomfort at the menstrual periods — a sensation of weight and heaviness in the pelvis, backache, headache, etc. Sooner or later, there is actual pain at the monthly periods, usually of a more or less colicky character.

As the condition advances to the development of hematocolpos, hematometra, and perhaps hematosalpinx, a tumor is observed in the lower abdomen. Even before this, in the ordinary case of imperforate hymen, there is a bulging at the site of the occluding membrane, which is pushed outward by the mass of accumulated blood behind it. In exaggerated cases pain and tenderness may be present continuously, due to the pressure of the tumor, and to the pelvic peritonitis which is often associated with it.

Chemical Composition of Retained Menstrual Discharge.— An analysis has been made by Bell of the retained fluid found in ten cases of hematocolpos. Mucin formed a large fraction, about one third of the fluid. Lactic acid was present in the absence of bacteria, and hence could not be due to the vaginal bacillus of Döderlein. Fibrin ferment and fibrinogen were absent, according to Bell, explaining the non-coagulability of the menstrual blood (Chapter VIII). The calcium content Bell found to be very great, while urea was absent.

Cause of Hematosalpinx in Cases of Gynatresia.— It is by no means as easy to explain the production of hematosalpinx as of hematometra or hematocolpos. The two latter conditions are obviously due to mere retention of menstrual blood. It is true that there are many who would explain hematosalpinx in the same manner, although this explanation takes for granted a doubtful point, viz., that the menstrual blood regurgitates into the tube, forcing its way through the normally tiny uterine orifice of the tube. Others believe that, while the blood in the hematosalpinx is mentrual blood, its source is not the uterus, but rather the tubal mucosa itself. As stated elsewhere (Chapter III), however, the best evidence is opposed to the theory of tubal participation in menstruation.

This difficulty is evaded by those who, like Pozzi, believe that in these cases the tubes assume a vicarious menstrual function, and that the bloody contents of a hematosalpinx represent a vicarious menstrual discharge. Another theory which may be mentioned is that the blood arises from the tubal wall either as a result of a circulatory disturbance or of an inflammatory reaction. The view of Mason and Bandl, that the blood has its source from ruptured graafian follicles, is too far fetched to merit serious consideration.

Diagnosis of Gynatresia.— In the great majority of cases the diagnosis is simple. The failure of menstruation to appear at the usual age,

when combined with the occurrence of definite menstrual molimina, should make one suspicious. The presence of an imperforate hymen can usually be determined by inspection. When the obstruction is higher up, the diagnosis may be more difficult. When taken together with the history, careful physical examination will usually determine the condition which exists. In cases of absence of the vagina or of vaginal atresia, bimanual examination, with one finger in the rectum, is often of great service.

Prognosis.— Gynatresia, with retention of menstrual fluid, must be looked upon as a serious condition. In former years the mortality was quite appalling. Fuld, in 1888, reported a mortality of 74 per cent in 65 cases. Of the 48 fatal cases, 9 died without operation having been performed. Such a mortality rate would not, of course, apply to the present day, but the condition is still fraught with no little danger. The principal complications to be feared are rupture of the sac, with perhaps fatal hemorrhage or shock, and peritonitis. The tubal fluid, for some as yet unexplained reason, is said by most authors to possess a disproportionate degree of infectiousness, and its expulsion into the abdominal cavity is therefore associated with great danger. Cases of spontaneous cure by rupture into the bladder or rectum, or through the septum of a double uterus, have been observed.

Treatment.— The treatment of the various forms of gynatresia which produce menstrual retention is surgical. The operation indicated depends upon various factors, but chiefly upon the location of the obstruction. The most common type, the imperforate hymen, is best treated by excision of the obstructing hymen under rigidly aseptic precautions. The technic of this, as well as of the other operative procedures indicated in other types of atresia, is described in the various text books of operative gynecology.

XIX

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CHAPTER XX

DYSMENORRHEA

General Considerations.— The term dysmenorrhea, literally translated, means difficult menstruation, and is applied to the condition in which there is pain at the time of the menstrual flow. In the normal healthy woman, the occurrence of the menses should be accompanied with little or no pain. In most women the menstrual periods are associated with certain subjective symptoms, the so-called menstrual molimina. At these times there is often a sensation of heaviness in the pelvis, general lassitude, sometimes headache, and often a condition of nervousness and increased irritability. Under ordinary conditions, however, these symptoms are not sufficient to inconvenience the woman to any extent. When, on the other hand, the occurrence of menstruation is characterized by more or less severe pain, the condition is spoken of as dysmenorrhea. There has been much discussion regarding the proper application of this term. There is no sharp dividing line between the moderate discomfort which so often accompanies normal menstruation, and the definite pain which constitutes dysmenorrhea. The individual factor obviously plays a most important rôle in determining the degree of such a purely subjective symptom as pain. As already stated, the word dysmenorrhea implies difficult or obstructed menstruation, and it is therefore looked upon by some as a misnomer, inasmuch as menstruation is often accompanied by great pain in the absence of any actual obstruction. For this reason the term "*menorrhalgia*" has been suggested by Massey as a substitute.

The most typical cases of dysmenorrhea are seen in the entire absence of any discoverable pathological lesion in the pelvis. There is no difference of opinion of the applicability of the term dysmenorrhea to such cases. On the other hand, pain at the time of the menstrual periods is often seen in women suffering with inflammatory or other disease in the pelvis, the extra congestion of the menstrual period appearing to provoke or accentuate the pain. The history of such cases often shows that there was no menstrual pain whatsoever before the occurrence of the pelvic lesion. There are some authors, notably Herman, who insist that the term dysmenorrhea cannot be properly applied to such cases, and that it should refer only to those cases in which there is no discoverable pelvic lesion, i. e., to those in which the cause appears to be intrinsically uterine. From the clinical point of view, at least, nothing is gained by making such a distinction. It seems more logical to apply the term dysmenorrhea to all instances of pelvic pain associated with

the occurrence of menstruation, and then to subdivide the cases into two principal groups, the primary and the secondary.

Types of Dysmenorrhea.— *Primary dysmenorrhea* may be defined as that form in which menstrual pain occurs in the entire absence of gross pathological lesions in the pelvis. *Secondary dysmenorrhea,* on the other hand, refers to those cases in which the pain at menstruation is associated with and apparently due to definite pelvic disease of one form or another. This division is of course based upon etiological considerations.

From a clinical viewpoint it is convenient to adopt Kelly's division of cases of dysmenorrhea into two types, which may be called the *spasmodic* and the *congestive*. In the former the "pain begins just before or exactly with the appearance of menstruation. It is sharp, well defined, and cramp like in character, coming on in paroxysms which last a minute or two and recur at short intervals." The suffering is not only more severe, but also of a different character from that accompanying normal menstruation.

In the congestive type, on the other hand, the pain appears to be an increase of the usual discomfort of the menstrual periods. "The pain begins from one to two days to a week before the appearance of the flow. It is of a dull, dragging character, extending all through the back and down the thigh, and is often accompanied by severe headache, occasionally associated with nausea, extreme lassitude, and nervous excitability. In some cases the symptoms are greatly relieved by the establishment of menstruation; in others, they continue throughout its duration."

The spasmodic form is especially characteristic of primary dysmenorrhea, and the congestive form is more common with the secondary type, although exceptions to this rule are not infrequent. Occasionally, both types of pain are present in the same patient.

Frequency of Dysmenorrhea.— Little importance can be attached to figures indicating the incidence of dysmenorrhea, inasmuch as, with regard to the secondary form at least, the frequency is largely dependent on the frequency of pelvic disease. In Chapter VIII are given the statistics of various authors of the frequency of pain at the time of menstruation. The fact that these statistics can take no account of the "personal factor" in dysmenorrhea, and, moreover, the fact that no attempt was made in such studies to separate primary and secondary cases, detracts a great deal from their significance.

CAUSES OF PRIMARY DYSMENORRHEA

General Considerations.— The extreme frequency of this form of dysmenorrhea, together with the severe pain and perhaps disability which it entails, has made it the subject of much study. This, however, has been almost entirely along clinical lines, and it cannot be said that much of real scientific worth has been contributed. The problem of the cause of primary dysmenorrhea is still unsolved, and it remains one of the big questions still

confronting gynecologists. Many theories have been suggested to explain the mechanism by which the pain is produced in these cases. In many instances more than one factor is, no doubt, concerned. According to the principal views regarding the causation of primary dysmenorrhea, one or more of the following factors may be concerned: (1) Mechanical obstruction of the uterine canal; (2) Hypoplasia of the generative organs; (3) Neuroses of one form or another; and (4) Constitutional diseases.

Mechanical Obstruction of the Uterine Canal.— It was at one time believed that dysmenorrhea is always due to some mechanical obstruction to the free exit of the menstrual blood. This belief dates from the time of Mackintosh, of England, who, in 1832, reported twenty-seven cases in which he had done dilatation of the uterine canal for the relief of the obstruction to which he attributed the dysmenorrhea. Twenty-four of these he reported to have been cured. This doctrine was greatly strengthened by the endorsement which it received from two of the greatest gynecologists of the time — Marion Sims and Sir James Y. Simpson. It was Sims who, in his classical paper entitled "Nulla Dysmenorrhea nisi Obstructiva," asserted that "there can be no dysmenorrhea, properly speaking, if the canal of the neck of the uterus be straight and wide enough to permit a free passage of the menstrual blood." In the same way, Robert Barnes, of London, stated "mechanical obstruction of the secretions is the most important factor in dysmenorrhea. The essential condition of dysmenorrhea is a retention of the menstrual secretion."

Even at the present time many text books and authors lay great stress upon the importance of mechanical obstruction in the production of dysmenorrhea. On the whole, however, this theory has been considerably shaken by numerous observations showing, on the one hand, that dysmenorrhea may occur in the entire absence of any mechanical obstruction, while, on the other hand, it may be absent where a greater or less degree of obstruction is present. Menstrual pain, for instance, is frequently present when the uterine canal is widely patulous. It has been shown that in cases of dysmenorrhea, supposedly due to cervical obstruction, a uterine sound may easily be passed through the cervical canal during the menstrual period, showing that there can be no very great obstacle to the free outflow of blood from the uterus.

The average amount of blood given off at each menstrual period is two to eight ounces, or, assuming that the menstrual flow lasts three or four days, not more than two ounces each day. This is equivalent to saying that about forty drops come through the cervical canal each hour, or two thirds of a drop each minute. It would seem difficult to conceive that the cervix in these cases of dysmenorrhea could be obstructed to such a degree as not to allow the passage of this small amount of blood. Furthermore, it is not uncommon to find severe dysmenorrhea in cases in which an excessively large amount of menstrual blood is passed.

Perhaps the principal argument in favor of the view that mechanical

obstruction may, at least in some cases, be responsible for dysmenorrhea is the fact that a certain number of cases of the primary form are relieved by dilatation of the uterus. On the other hand, an even larger number are not relieved at all, or are improved only temporarily. Moreover, when the genital canal is actually obstructed, as in gynatresia, the resulting pain is rarely of the type seen clinically in cases of spasmodic dysmenorrhea. Certainly it is rarely so severe.

Relation of Anteflexion to Dysmenorrhea.— In the majority of cases of primary dysmenorrhea, the uterus is anteflexed, and it is the anteflexion which is commonly believed to cause the obstruction or "kink" in the uterine canal. The association of anteflexion with dysmenorrhea has been studied by many authors. The conclusions of Herman on the subject represent the opinion of the majority of the leading authorities. They are as follows:

"First: There is no anatomical evidence that anteflexion causes any appreciable hindrance to the escape of menstrual fluid.

"Second: There is reason to think that well marked anteflexion is present in nearly one half of all women who have not borne children.

"Third: Therefore, it is to be expected that anteflexion and dysmenorrhea would frequently coincide.

"Fourth: Dysmenorrhea is practically as common when the uterus is anteflexed as when it is not.

"Fifth: When dysmenorrhea and flexion go together, the severity of the pain bears no relation to the degree of the bending.

"Sixth: Dysmenorrhea associated with anteflexion is frequently cured without straightening the uterus.

"Seventh: There is no evidence that straightening the uterus invariably or frequently removes dysmenorrhea which is associated with anteflexion, and in which other methods of cure have been ineffectual.

"Eighth: These facts tend to show that the relation between anteflexion and painful menstruation is not that of cause and effect, but that of coincidence."

Hypoplasia of Reproductive Organs.— Closely related to so-called obstructive dysmenorrhea is that form which is so frequently associated with defective development of the pelvic organs. Even in women who are otherwise robust and well developed, it is not rare to find the uterus small and hypoplastic, and perhaps distinctly infantile in type. (Fig. 30.) The infantile character of the uterus in these cases is further shown by the fact that it is frequently anteflexed. It will be remembered that the uterus of the female fetus or infant is often anteflexed, so that conditions in which the uterus remains very small and anteflexed may be looked upon as representing an arrest of development.

From our present standpoint these cases are of interest because they are quite characteristically associated with more or less severe dysmenorrhea. Incidentally, it may be said that sterility is also found in the majority of such

cases. These three manifestations — infantile uterus, dysmenorrhea, sterility — constitute a triad familiar to every practicing physician on account of the frequency of its occurrence. This is one of the most interesting forms of dysmenorrhea with which we have to deal, and at the same time the most intractable, on account of the fact that so little is known concerning the exact mechanism of its production.

Various theories have been suggested to explain the pain observed in these cases. There are some who believe that the dysmenorrhea seen in these cases is to be looked upon as obstructive in type; in other words, that it is due to the cervical stenosis, or the kink in the cervical canal produced by the sharp anteflexion. Others, again, suggest that it is due to the fact that at the time of menstruation the endometrium undergoes marked swell-

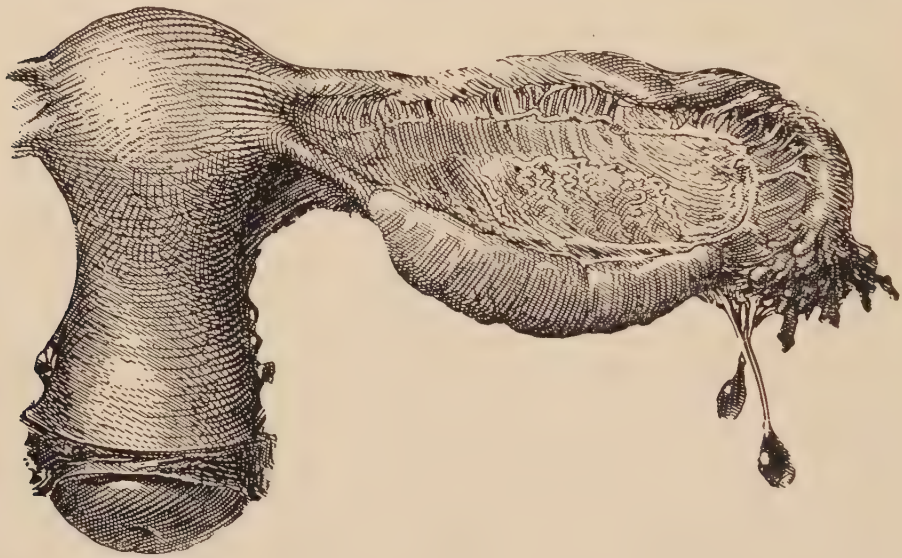

Fig. 30.— An Elongate Infantile Ovary With Puerile Type of Uterine Body (Kelly).

ing and congestion, the small uterine cavity being unable to accommodate this hypertrophied endometrium. Still others believe that it is the dilatation of the blood vessels in the muscularis rather than the swelling of the mucous membrane which is responsible for the pain.

The theory of an obstructive origin of the pain, as we have already seen, is no longer tenable. The investigations of Schultz tend to support the view that dysmenorrhea of the type now under discussion is due to what may be called the vascular tension resulting from deficient calibre of the uterine vessels.

This investigator states that up to the age of puberty the uterus has the form of the "infantile" uterus, as we find it clinically in association with spasmodic dysmenorrhea. Under normal conditions the uterus at puberty enters upon a process of development continuing up to about the twentieth

year, when the full maturity of the organ is attained. The mature uterus contains a preponderance of muscle over connective tissue, unlike the immature organ, in which the proportion between connective tissue and muscle is that of two to one. In cases of "infantile uterus," associated with spasmodic dysmenorrhea, there has been a retardation of development in the organ, so that, like the undeveloped uterus, it contains a preponderance of connective tissue.

The normal hyperemia of menstruation causes an engorgement of the uterine vessels, producing what Schultz describes as a capsular distention of the connective tissue layers in which are contained the blood vessels. Owing to the deficiency of muscle tissue in the uterine wall, there is a stagnation of the blood in the uterine veins. This venous stasis gives rise to pressure stimulation of the uterine nerves, and thereby to the characteristic spasmodic labor-like contractions which are responsible for the pain.

Some recent studies which I have made, on the menstrual reaction of the endometrium in various types of pelvic disease, have seemed to me to throw some light on this question. In a clinical and anatomical investigation of a large series of cases from the gynecological department of the Johns Hopkins Hospital, I was able to demonstrate that, generally speaking, the degree of premenstrual hypertrophy in the endometrium is proportionate to the clinical severity of the menstrual bleeding, with the exception of one important group, the cases of congenital anteflexion of the uterus.

In these, even though menstruation is usually rather scanty, the menstrual reaction is often noted unusually early in the menstrual cycle, and may become very marked. This is rather surprising, since we are accustomed to look upon these cases as representing a greater or less degree of arrested development. In some of my cases the uterus was distinctly infantile in type. Menstruation was much more frequently scanty or moderate than profuse. Dysmenorrhea was observed in practically all the cases, and in those of the patients who were married sterility was almost invariable.

Since the histological reaction of the hypoplastic uterus to menstruation is certainly not any less than that of the normal organ, the question arises as to why menstruation is usually scanty in the hypoplastic cases. If it be true, as the study of my series seemed to indicate, that in congenital anteflexion there is no impairment of ovarian activity, the idea suggests itself that perhaps in these cases there is just as great a degree of menstrual hyperemia of the endometrium as in those in which the uterus is well developed, but that in the former it is the local factor which is defective; in other words, that there is a physiological as well as an anatomical deficiency in the uterus. This local factor, it is commonly believed, exerts its effect principally on the blood vessels, rendering them permeable to the passage outward through their walls of the blood elements. In these cases menstruation may be much less than the average because the blood elements do not pass out from the blood vessels with the same facility as in the entirely normal uterus. This hypothesis would seem to explain the characteristic pain

observed in cases of this type, for an engorged endometrium, unrelieved by menstrual discharge of blood elements, might be expected to act as a stimulant of uterine contractions, much as a foreign body would. This conception is given further plausibility by the characteristic relief from pain which is noted as soon as the menstrual flow is well established. The problem as a whole, however, must still be considered unsolved.

In conclusion, it may be emphasized that dysmenorrhea is more frequently observed in the milder grades of uterine hypoplasia than in those of marked degree. In the extreme cases, *uterus rudimentarius* or *uterus fetalis* (Fig. 31), amenorrhea is the rule. In patients with uteri of the genuinely infantile type, *uterus infantilis* (Fig. 32), menstruation is characteristically scanty, while dysmenorrhea may or may not be a symptom. In the relatively slight degrees of uterine hypoplasia, as represented by what I have called the *uterus*

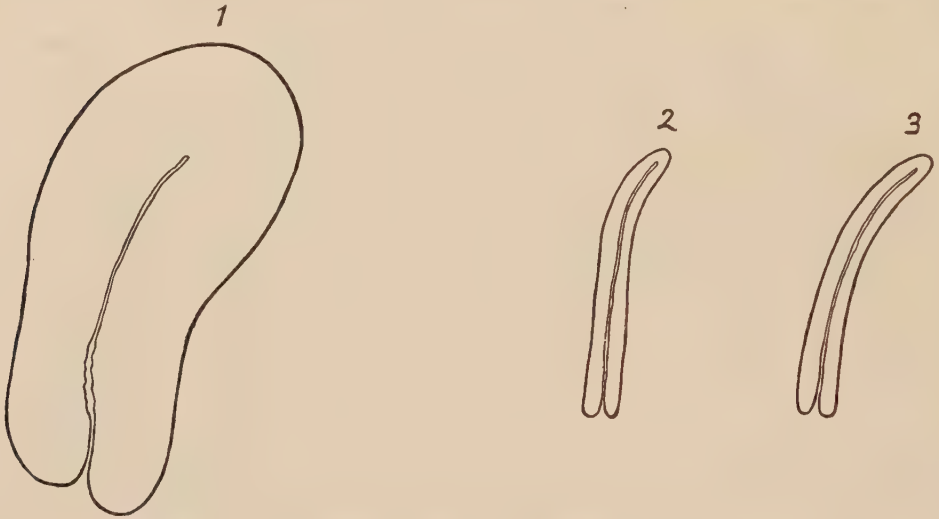

Fig. 31.— The Fetal Type of Uterine Hypoplasia (Uterus Rudimentarius or Fetalis), 2 and 3, as Compared With the Normally Developed Uterus, 1.

subpubescens (Fig. 33), dysmenorrhea is the characteristic symptom, the amount of the flow being either normal, deficient, or excessive. For a fuller discussion of these types of uterine hypoplasia and their relation to dysmenorrhea, the reader is referred to a recent paper by the author on "Infantilism and Other Hypoplastic Conditions of the Uterus." (See Bibliography.)

Role of Neuroses in Causation of Dysmenorrhea.— A third type of primary dysmenorrhea which is not infrequently encountered is that in which the menstrual pain is of distinctly neurotic origin. It is not usually easy to distinguish these cases with precision from those due to the causes which have already been described, especially since patients suffering from dysmenorrhea due to hypoplasia are frequently highly neurotic as well. The cases coming under this group may be classified under three headings, hysterical, neurasthenic, and neuralgic.

Hysterical Dysmenorrhea.— With regard to hysterical dysmenorrhea, it must be emphasized that this diagnosis should never be made in the absence of the well known earmarks of hysteria, such as hemianopsia, paresthesia, anesthesia, etc. Hysteria is looked upon by neurologists as a disease of the cerebral cortex, which may exhibit local manifestations in various organs, including those of the pelvis. A well known teacher is

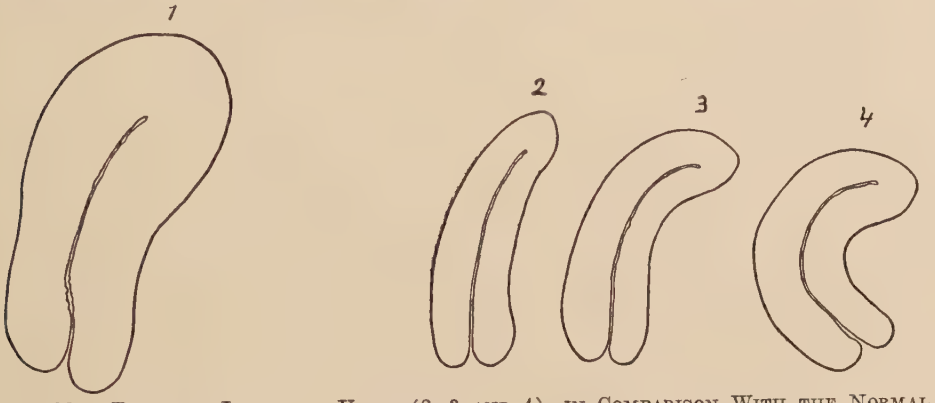

Fig. 32.— Types of Infantile Uteri (2, 3 and 4), in Comparison With the Normal Uterus (1).

In all the cervix predominates over the corpus. In 3 is shown a moderate corporeal anteflexion, while 4 illustrates the more characteristic cervicocorporeal anteflexion. In some cases the cervix is normal, in others long and conical, with pinhole os. Uteri of infantile type may be of practically normal size, or they may be considerably smaller.

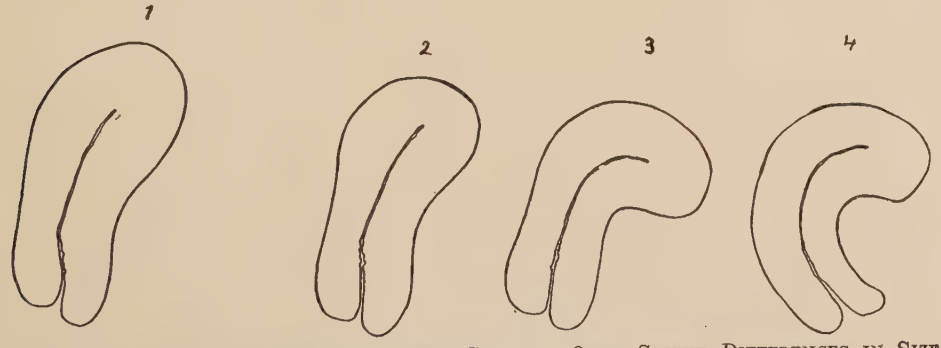

Fig. 33.— Types of Subpubescent Uteri, Showing Only Slight Differences in Size from Normal Uteri (1).

In 2, 3 and 4 are shown, respectively, corporeal and cervicocorporeal anteflexion.

quoted as having made the statement that hysteria may be excluded, if the pain is fixed. Nothing could be more fallacious than this statement. Every gynecologist is familiar with the picture of the hysterical woman who complains, perhaps bitterly, of pain in the region of the ovary, even when the most careful examination fails to reveal any pathological lesion. In the same way, the hysterical patient may suffer with intense dysmenorrhea

occurring with each period, even when the pelvic organs are in themselves absolutely normal. The dysmenorrhea in these cases is very often accompanied by hysterical convulsions or other manifestations of characteristically hysterical nature. These troublesome cases are most frequently observed in young girls. Many of these patients are obliged to take to bed every month. It is especially just before and on the first day of the flow, that the symptoms are apt to be most severe, the patient often screaming and tossing about in a very unmanageable manner.

Dysmenorrhea of Neurasthenic Origin.— Neurasthenic dysmenorrhea is quite different in the manner of its production — just as different as is neurasthenia from hysteria. Neurologists divide neurasthenia into a primary and a secondary form. The *primary* variety is the result of such factors as heredity, environment, mode of life, etc. As the term itself indicates, it is characterized by a condition of general weakness or asthenia of the nervous system, with symptoms of the most varied character referable to any part of the body. Frequently it is the pelvic organs that bear the brunt of the neurasthenic condition, the most frequent symptom being dysmenorrhea. In these cases it is usually associated with a greater or less amount of pelvic pain in the intermenstrual period. The pelvic organs themselves are often normal in these cases, the dysmenorrhea representing merely a reflection of the patient's general condition of neurasthenia. When the latter is improved, the dysmenorrhea is also usually relieved.

Many perplexing problems may arise when dysmenorrhea is seen in neurasthenic women who, at the same time, have some distinct pathological lesion in the pelvis. The problem in these cases is to determine whether the dysmenorrhea is directly caused by the pelvic lesion, which may perhaps be slight, or whether it is only a part of the neurasthenia. Furthermore, it must be ascertained, if possible, whether the neurasthenia in these cases is primary, or whether it is secondary to some underlying condition, either intra- or extrapelvic.

Secondary neurasthenia is the form which is brought about by some underlying condition, usually some definite anatomic disease. A woman with a normal, well developed nervous system, for instance, may, after long years of suffering from some chronic disease, be reduced to a condition in which her entire nervous system is undermined, resulting in secondary neurasthenia. The same result may, of course, be seen after disease in other parts of the body as well as in the pelvis. In the dysmenorrhea which is frequently found when a condition of neurasthenia has been superimposed upon one of original pelvic disease, both factors must be considered in explaining the production of the dysmenorrhea or in attempting its relief.

Even if the lesion in the pelvis be removed, women of this type often suffer with menstrual pain to the same degree as before operation. This is due to the fact, of course, that the condition of neurasthenia still persists and must be corrected before any relief from the dysmenorrhea can be expected. In other words, the neurasthenia in these cases may be looked

upon as just as true a complication of the pelvic disease as peritonitis is of appendicitis. Even after the ruptured appendix has been removed we may still have to contend with the condition of peritonitis. In the same way, even after diseased pelvic viscera have been removed, we may still have to deal with the superimposed condition of neurasthenia.

Neuralgic Dysmenorrhea.— The third variety of dysmenorrhea of distinctly nervous origin is the neuralgic form. In former years the diagnosis of ovarian neuralgia or oöphoralgia was a rather common one. Patients of this group complained of sharp shooting pains over one or both ovaries, occurring at irregular periods, sometimes during the menstrual epoch, sometimes in the intermenstrual period. In the broad sense in which we have used the word dysmenorrhea, cases of this kind might perhaps be spoken of as neuralgic dysmenorrhea. The neuralgic pains in these cases appear to be analogous with those so frequently seen in the supra-orbital or intercostal nerves. Neurologists, however, are still in the dark in regard to the true nature of neuralgia, and, especially as applied to the pelvic organs, this term should be used only with the greatest caution, if at all.

CAUSES OF SECONDARY DYSMENORRHEA

General Considerations.— This form of dysmenorrhea may be the result of almost any of the numerous forms of local disease of the reproductive organs. It is scarcely necessary to say that in the individual case it is not always easy to distinguish between primary and secondary dysmenorrhea, inasmuch as the mere presence of a pelvic lesion is not conclusive evidence that it is the cause of dysmenorrhea, if the latter exists. The definition of secondary dysmenorrhea indicates that constitutional diseases cannot be looked upon as direct causes. Undoubtedly, however, they are in many instances contributory or predisposing factors of great importance, especially in their influence upon the severity of the menstrual pain.

Constitutional Disease as a Predisposing Factor.— Speaking generally, any condition which brings about a deterioration of the general health and a lowering of body resistance may be associated with the occurrence of dysmenorrhea. Aside from actual disease, the poor vitality so often due to bad hygienic surroundings, physical or mental overwork, lack of proper sleep, and other such factors frequently "lowers the threshold" to pain stimuli. The slight pelvic discomfort commonly observed with normal menstruation may thus be magnified to an actual pain of greater or less severity.

Chlorosis and Other Forms of Anemia.— Of the constitutional diseases which may cause dysmenorrhea, chlorosis and other forms of anemia are worthy of special mention. According to Virchow, hypoplasia of the uterus is one of the anatomic characteristics of chlorosis, and this fact may explain the frequent occurrence of dysmenorrhea in thoses cases of this disease in which menstruation does not disappear entirely. The general debility characteristic of the disease, however, is a contributing

factor of much importance in the production of the menstrual pain in these cases. The same thing is true of other forms of anemia.

Tuberculosis.— Of especial interest is the dysmenorrhea which is so frequently observed in cases of tuberculosis, even in an incipient stage. While this is in part explainable by the anemia and lowered vitality which often mark the course of this disease, it is of interest to note that some authors would explain the dysmenorrhea as more directly the result of the tuberculous disease.

Eisenstein and Hollos record that one hundred and eighteen women with menstrual disturbances gave a positive reaction to tuberculin, although there was nothing else to suggest the existence of tuberculosis. In fifty-three such patients in whom no other cause could be found for the dysmenorrhea, and who were subjected to a course of tuberculin treatment, forty were definitely relieved, five showed only slight improvement, while in eight there was no improvement. In a few cases which subsequently came to autopsy, tuberculous lesions were discovered. Cases of this latter type can scarcely be classified as primary dysmenorrhea, inasmuch as definite local pathological conditions were present. The same statement may be made concerning the case reported by Pfannenstiel, in which rapid miliary tuberculosis in the abdomen followed dilatation of the cervix by laminaria for the relief of dysmenorrhea.

Gräfenberg obtained a positve tuberculin reaction in twenty-one of thirty patients who had applied for relief from primary dysmenorrhea. In cases of secondary dysmenorrhea, the response was always negative. In cases of the primary group the genitalia, according to Gräfenberg, are always underdeveloped. In eleven of his cases there was also a local reaction in the genitalia after the use of tuberculin. These findings lead him to believe that the defective development of the genital organs so aften associated with dysmenorrhea is the result of a tuberculous process which involves the pelvic organs during childhood, later undergoing healing.

In a similar study of this relationship, Cotte finds that the majority of women who suffer with tuberculosis exhibit dysmenorrhea. In a series of seventy such women whom he treated with tuberculin, he reports forty as cured of the dysmenorrhea. He considers the dysmenorrhea as definitely due to a toxemia of tuberculous origin. Much more evidence is needed, however, before there can be any acceptance of the views of either Cotte or Gräfenberg.

Other Constitutional Disorders.— Among the other constitutional disorders with which dysmenorrhea may be clinically associated, mention may be made of diabetes, nephritis, syphilis, rheumatism, gout, and chronic cardiac disease.

Dysmenorrhea Due to Local Pelvic Disease.— There are few pelvic disorders which may not at times be associated with dysmenorrhea. In an analysis of 1000 cases admitted to the gynecological wards of the Johns Hopkins Hospital, omitting those in which menstruation had ceased or had

not yet begun, Holden found that dysmenorrhea was present in 47 per cent. This series, it may be added, included also those patients with rectal, renal, and ureteral disease. In about 23 per cent of the entire number, the dysmenorrhea seemed to be definitely caused by certain abnormal conditions of the pelvic organs. In 22 per cent, it was present in conjunction with such conditions, but was apparently not caused by them. It is interesting to note that in about 90 per cent of all the cases of secondary dysmenorrhea, the cause is to be found in one of three conditions: (1) retrodisplacements of the uterus; (2) pelvic inflammatory disease; and (3) myomata of the uterus.

Retrodisplacement of Uterus.— This, according to Holden, is the most frequent cause of dysmenorrhea, accounting for fully forty-one per cent of the cases. Of nulliparous women with displacements which cause symptoms, 86 per cent suffer with dysmenorrhea. In the cases of retrodisplacement which occur after childbirth, dysmenorrhea is much less common. About 25 per cent of the nulliparae have dysmenorrhea which is apparently caused by malposition. In an analysis of 176 cases of retroversion, Judd found that 59 per cent suffered with dysmenorrhea.

Inflammatory Disease of Pelvic Organs.— About 37 per cent of the cases of dysmenorrhea in Holden's series were found to be due to inflammatory disease of the uterus, tubes or ovaries. In the majority of these, the inflammation was of a chronic type. Endometritis, contrary to the older teaching, is an infrequent cause of dysmenorrhea. This is not surprising when one considers the comparative infrequency of this condition. Cullen, for example, found a genuine endometritis in only forty-eight of eighteen hundred microscopic examinations of the endometrium.

As regards the relation of pelvic inflammatory disease to dysmenorrhea, one is frequently struck with the disparity between the pathological findings in the pelvis and the degree of menstrual pain of which the patient complains. It is remarkable how much trouble may exist in the pelvis in women, compatibly with a fair measure of comfort. Not infrequently bimanual examination may show the presence of large pus tubes, while little or no dysmenorrhea or pelvic pain is complained of by the patient. On the other hand, a catarrhal salpingitis, with very little enlargement of the tubes, may give rise to extremely severe pain with the periods.

I may cite the case of a young woman who came under my observation, and who complained of intense pain at each menstrual period. Bimanual examination failed to reveal any very definite pelvic disease. She had already passed through the hands of two competent gynecologists and had been dismissed as a neurasthenic. The severity of the pain led me, in consideration of the patient's apparently well balanced nervous system, to advise operation, in spite of the absence of palpable pelvic disease. Double chronic salpingitis was found, the moderately thickened tubes being adherent very high up near the brim of the pelvis, so that they were difficult to out-

line through the rather thick abdominal wall, even under anesthesia. Removal of the diseased tubes cured the dysmenorrhea.

Myomata of Uterus.— In the series studied by Holden, myomata were found to be the cause of dysmenorrhea in 11 per cent. Kelly has also collected the records of two hundred cases of myoma, under the age of forty-five, from the Johns Hopkins Hospital, for the purpose of determining the frequency of dysmenorrhea with this condition. Ninety-four of his cases were white and one hundred and six colored. He found that in 25 per cent dysmenorrhea had been noted since the onset of the patient's trouble. He alludes to a similar study made some years previously, in which dysmenorrhea was observed in 20 per cent of the cases.

As might be expected, dysmenorrhea is much more frequently encountered with myomata of the submucous or interstitial type than with the subperitoneal variety. This is obviously due to the fact that myomata of the first two varieties are especially apt to excite expulsive uterine contractions, and at the same time are more frequently associated with congestion of the uterine mucosa and muscularis.

Other Forms of Pelvic Disease.— From the study of Holden it would appear that about 11 per cent of all cases of dysmenorrhea were caused by various forms of pelvic disease other than the three important groups already discussed. It is scarcely necessary to enumerate these remaining possible causes of dysmenorrhea, inasmuch as they embrace practically all the usual forms of pelvic disease, such as polypi, cystic or solid tumors of the ovary, carcinoma, etc.

CLINICAL CHARACTERISTICS OF DYSMENORRHEA

Clinical Types.— Pain of any kind is a purely subjective symptom, and is therefore subject to the widest individual variations. This is preeminently true of pain at the time of menstruation. It is necessary only to mention the principal types of pain experienced by women at the time of menstruation, bearing in mind that numerous factors may operate to modify these types in one way or another. The great majority of cases of dysmenorrhea may be classified under one of the two principal types distinguished by Kelly, i. e., the spasmodic or the congestive forms.

Spasmodic Dysmenorrhea.— This is well typified in those very frequent cases of primary dysmenorrhea seen in nulliparous young women, often associated with scanty menstruation and frequently, in married women, with sterility. Such women, in the interval between menses, may enjoy perfect health. One or sometimes two days before the onset of menstruation, however, they begin to suffer with severe spasmodic pains in the pelvis. Sometimes the spasmodic character of the pain is conspicuous, so that the comparison to miniature labor pains is justified.

In other cases, the pain is somewhat less intermittent. It often radiates toward the back or down the lower limbs. It may be associated with nausea or vomiting, suggesting a toxic origin. In neurotic individuals

there may be well marked nervous symptoms. In some cases these take the form of depression, in others, especially those of hysterical tendencies, there may be marked excitability, and perhaps even convulsions.

The pain continues with greater or less severity until the flow is well established, when it usually abates, sometimes quite suddenly. While the pain commonly ceases after the first day of the bleeding, it may continue longer, and perhaps throughout the entire period.

Congestive Dysmenorrhea.— While this form of pain is sometimes encountered in primary dysmenorrhea, it is more frequent in cases of the secondary type. The time at which it appears is subject to wide variation. It may begin as much as a week before the onset of the menstrual period, or it may not occur until the first day of the flow. Occasionally, as a matter of fact, it is only toward the end of the menses that pain is complained of. Efforts to correlate the time of appearance of the dysmenorrhea with the type of pelvic lesion have not been very satisfactory.

The pain is usually of a dull, dragging, or bearing down character. In secondary dysmenorrhea it is often more marked on one side than on the other, and may be perceived on one side only. Usually, of course, this is the side of the pelvic disease, although this is not an invariable rule. Frequently the pain in the iliac regions is accompanied by backache, and perhaps by pain in the limbs.

Other symptoms may be associated, such as headache, nervous irritability, and digestive disorders, together with the various manifestations of the causative pelvic disease.

TREATMENT OF DYSMENORRHEA

General Considerations.— The relief of menstrual pain during a specific attack of dysmenorrhea is usually simple enough, consisting in the mere relief of pain. The radical treatment of dysmenorrhea, however, looks to permanent relief from pain at the menstrual periods. The treatment of dysmenorrhea may therefore logically be considered under two heads: (1) symptomatic treatment of dysmenorrhea during an attack; and (2) treatment for permanent relief of the dysmenorrhea.

Treatment During Attack.— General Measures.— Except in the milder grades of dysmenorrhea, rest in bed is of great importance in the relief of the pain. When the dysmenorrhea is severe, it is usually unnecessary to enjoin this, as the patient takes to bed of her own accord. In the mild forms of dysmenorrhea, rest in bed is frequently all that is necessary to relieve the pain. When the condition is more severe, however, other measures are necessary. The bowels should be well evacuated. When the pain is quite severe, a hot water bag to the lower abdomen often gives much relief.

Drugs.— The drugs which have been employed in the treatment of dysmenorrhea are legion. Among the most valuable I would place the various coal tar derivatives, such as phenacetin, acetanilid and antipyrin. Of these,

phenacetin is perhaps the most desirable, since it is the least depressing. In administering any of these drugs, due regard must be paid to the condition of the patient's heart, and caffein should be combined with the analgesic. Either of the following simple prescriptions will be found serviceable in many cases:

℞ Acetphenetidin. . . . . ʒ i
Caffeinae. . . . . gr. vi
Sod. bicarbonat. q. s. . . . . ʒ ii
M. et div. in chart. no. xii.
Sig. One powder with water q 3 hours.

℞ Acetanilidi. . . . . gr. xlv
Caffeinae. . . . . gr. vii ss
M. et div. in caps. no. xv.
Sig. One capsule every three hours.

Closely allied with the coal tar derivatives are such drugs as aspirin (ac. acetylsalicylic) and pyramidon (dimethylaminantipyrin). The former may be prescribed in tablet form in doses of five grains every four hours. Pyramidon is best given in capsule form in doses of three to six grains every four hours.

Occasionally the pain is so severe that it may be necessary to add small doses of codein to any of the above drugs, as in the following prescriptions:

℞ Acetanilidi. . . . . gr. xlv
Caffeinae. . . . . gr. vii ss
Codein. sulphat . . . . . gr. iii
M. et div. in caps. no. xv.
Sig. One capsule every three or four hours.

According to Matthews Duncan, the best drug in the treatment of dysmenorrhea is guaiacum, given in doses of ten grains three times a day, beginning a week before the onset of menstruation.

The two drugs, however, which are most efficacious in relieving the pain of dysmenorrhea both possess such serious disadvantages that they should rarely, if ever, be employed. I have reference to morphin and alcohol. The administration of either is attended with the risk of habituation to their use, especially when they are used in the treatment of such a regularly recurring trouble, as dysmenorrhea so frequently is. In rare instances, where the cramp-like pains are very severe, opium may be given guardedly, as in the following prescription recommended by Hirst:

℞ Tinct. opii. camph. . . . . ʒ i
Tinct. zingib. . . . . ʒ i
Spir. chloroform . . . . . ʒ ii
Syrup acac. . . . . ʒ ss
Aq. menth. piper. qs. ad. . . . . ʒ iv
M.
Sig. One tablespoonful when required for cramps.

I have often obtained quick results from the use of belladonna, in suppositories containing a half grain of the extract. In severe cases, the extract of opium, in doses of a quarter of a grain, may be combined with the belladonna.

In cases characterized by marked nervous symptoms, it is usually advisable to resort to the administration of bromids. Since there is very little pain relieving virtue in the bromids themselves, they must usually be combined with some more decidedly analgesic drug.

A number of vegetable drugs have been credited, probably wrongly, with more or less efficacy in relieving dysmenorrhea. Among these apiol is perhaps the best known. Its principal indication would seem to be in those cases of dysmenorrhea associated with scantiness of the flow. It is administered in doses of from three to six minims three or four times a day. On account of its disagreeable taste, it is best given in capsules.

Still another drug often employed, though of doubtful value, is viburnum prunifolium, in the form of the fluidextract, which may be given in doses of twenty minims to one dram. The National Formulary includes a preparation, the elixir of viburnum prunifolium (elixir viburni prunifolii), which is given in doses of one dram, and which is much less disagreeable than the official fluidextract. Certainly, if this drug is employed at all, there is no need to resort to the various proprietary preparations which have such wide vogue, and which in addition to viburnum prunifolium contain usually an array of little known drugs with long sounding names, but which are therapeutically worthless.

Hydrastis is another drug often resorted to in the treatment of dysmenorrhea. The fluidextract is the best form in which to administer it, the dose being from ten to thirty minims, given well diluted in water.

Some of the most widely used of the proprietary mixtures purport to depend for their antidysmenorrheic properties upon the presence of such drugs as helonin. It has been demonstrated, however, that the therapeutic effect of this drug is practically nil. Incidently, the preparations in question contain a large proportion of alcohol. When one considers that the dose recommended in severe dysmenorrhea is often a teaspoonful every ten or fifteen minutes, it can be readily understood that any relief which such a preparation affords is probably to be attributed to the alcohol it contains. The dangers of prescribing such remedies are obvious.

A number of other drugs have been used in the treatment of painful menstruation. Many of them are of doubtful efficacy, but some are even now quite extensively used. Thus may be mentioned cannabis indica, in doses of twenty or thirty drops of the tincture; pulsatilla, in doses of three minims of the fluidextract; piscidia erythema, in doses of one half to two drams of the fluidextract (Hare), and gelsemium in doses of ten or fifteen minims of the tincture.

The Atropin Treatment of Spasmodic Dysmenorrhea.— The employment of atropin in the treatment of spasmodic dysmenorrhea is, in my

opinion, entitled to the emphasis of special consideration. Unlike the other drugs which have been enumerated, atropin seems to fulfill a real indication, other than the mere relief of the symptom of pain. The form of dysmenorrhea in which atropin is of value is the spasmodic, which is observed so characteristically in young nulliparous women, and which is frequently associated with scanty menstruation, and sometimes with sterility. We are all familiar with the clinical picture of such cases. The use of atropin in the treatment of this form of dysmenorrhea is based on the fact that it diminishes the irritability of the autonomic nerve endings in the uterus. In 1910, Drenkhahn reported remarkable results from the injection of a solution of atropin directly into the cervical canal (1 mg. of atropin in 1 c.cm. of water). If a speculum or syringe be not at hand, he advised the introduction of a tampon saturated with atropin solution (1 per cent strength). This plan of treatment, Drenkhahn states, he had followed for fifteen years, basing it originally on the experimental work of Schindler, who showed that atropin has a direct action on the uterine muscle.

The method was taken up by Novak, of Vienna, who was struck by the fact that many women with increased irritability of the autonomic nerve system suffer with dysmenorrhea. In accordance with the *Krämpftheorie,* he suggested that the dysmenorrhea is due to the increased irritability of the autonomic nerve endings in the uterus. Novak administers the atropin in pills containing 0.5 mg. each, three being given each day, beginning just before the expected onset of menstruation. His preference for the administration of the drug by mouth is a wise one, for the results appear to be just as satisfactory as by Drenkhahn's method, while he thus avoids the slight danger of infection associated with the latter. Novak's method is obviously less disagreeable, especially in the case of virgins.

Thirty-eight cases were reported by Novak, in thirty of which the results were distinctly favorable. All these patients had suffered with "crampy" pains, except one in whom the pain was rather continuous, and one in whom the character of the pain is not mentioned. In the thirty favorable cases the pain either disappeared entirely or else became insignificant. The less characteristic symptoms which so frequently accompany the spasmodic pain — backache, bearing down in the lower abdomen, general lassitude, etc. — were not influenced by the atropin, which seemed to exert a special effect on the colicky pains. In one case the result was rather indefinite, the patient being better, but not strikingly so. In seven cases the treatment failed to relieve the pain. Among these seven were the two mentioned above as atypical, that is, not suffering with the spasmodic pains of typical "menstrual colic."

Novak is inclined to believe that failures, when they occur, are due to insufficient dosage. This would seem to be in conformity with the experimental work of Kehrer, who found that in small doses atropin stimulates the uterine muscle, while in large doses it inhibits it.

Stolper, who has also employed the atropin method in a large number of

cases, offers a different explanation for the failures which occur in a certain proportion of cases. He asserts that atropin is very efficient in those cases in which the dysmenorrhea is accompanied by other vagotonic symptoms. In a certain number of dysmenorrheics, however, vagotonic symptoms are absent, and, according to Stolper, there may even be symptoms indicating a heightened irritability of the sympathetic system (sympathicotony). As a means of clinical differentiation between these two groups, he lays much stress on a study of the blood pressure. He lays down the rule that women with a normal or slightly raised blood pressure react most promptly to atropin, while when the blood pressure is greatly raised there is apt to be no response to the administration of atropin. The blood pressure must be measured in the intermenstrual interval, not during menstruation or during the premenstrual period. Stolper, I may add, administers the drug either in suppositories (0.001 gm.) or by subcutaneous injection (0.00075 gm.).

My own experience with the atropin treatment of spasmodic dysmenorrhea has been most encouraging. In the frequent cases of young unmarried women in whom pelvic examination is obviously undesirable, and who present the classic picture of spasmodic pain recurring with each menstruation, the atropin treatment is indicated without the preliminary of pelvic examination. In my own cases I have followed the plan of Novak, though I have frequently administered somewhat larger doses than those recommended by him. My experience has been that the cases which respond most favorably are, speaking generally, those in which the atropin has been pushed to the point of tolerance. The plan has been to commence the administration of the drug about two days before menstruation is expected to appear, and to continue its use until the second or third day of menstruation, depending on the usual duration of the pain. Patients differ, of course, in the degree of tolerance to the drug. Ordinarily, about 1/100 grain is given three times a day, unless some pain appears, in which event, if there are no symptoms of atropin saturation, the doses may be given somewhat more frequently. Many patients complain of dryness of the throat, itching of the skin, and sometimes even disturbed accommodation, in which case it may be necessary to lessen the dosage somewhat. When it is desired to study the effect of the atropin on dysmenorrhea, it is best to administer it alone, as in tablet form. In some cases, however, I have combined it with various other drugs of analgesic nature, such as aspirin. Other than the occasional symptoms due to overstepping the patient's atropin tolerance, I have observed no bad results of any kind.

The results in the cases of spasmodic dysmenorrhea which I have treated with atropin have been very encouraging — so much so as to impel me to further employment of the method. While there have been some failures, there have been, on the other hand, some strikingly successful results. For the failures I have no explanation to suggest other than those quoted above from Novak and Stolper. It is hardly necessary to add, in conclusion, that it would be illogical to expect good results from the administration of

atropin in cases of dysmenorrhea associated with definite pathologic lesions in the uterus or adnexa. In such cases the logical treatment of the menstrual pain is the removal or treatment of the causative lesion.

Treatment by Benzyl Benzoate.— Recently Macht has urged the use of benzyl benzoate as an antispasmodic in a number of diseases, including uterine colic. Litzenberg has reported favorably on this plan of treatment in a series of cases of spasmodic dysmenorrhea. The mode of action of the benzyl benzoate is stated to be similar to that of atropin, the advantage over the latter lying in its non-toxicity. Benzyl benzoate is administered in the form of an alcoholic solution in doses of twenty to thirty drops every four hours, although considerably larger doses are believed to be safe by Litzenberg. To avoid the rather disagreeable taste of such a solution, Litzenberg recommends the use of the aromatic elixir of eriodictyon as a vehicle. He employs the following formula:

Benzyl benzoate	10 gms.
Mucilage of acacia.....	5 gms.
Aromatic elixir of eriodictyon.....	35 gms.

Sig. Give from one half to two teaspoonfuls, according to necessity.

The Mammary Treatment of Dysmenorrhea.— In 1907 Polano, on the theory that the ovaries and mammae are antagonistic in their physiological activities, suggested the treatment of dysmenorrhea by inducing hyperemia of the breasts. When the latter are doing extra work, as during pregnancy and the puerperium, the ovaries are resting. The physiologic work of an organ is dependent on its blood supply, and the method of Polano aims to bring about overfunction of the breast by means of suction hyperemia. He thus seeks to give the ovaries rest. He claims that the results of the treatment have been surprisingly good in a number of cases which had showed no benefit under other plans of treatment.

A few days before the menstrual period is due a suction glass is applied to each breast, as in the treatment of mastitis. The air is aspirated with a syringe until the breast is drawn out, stopping short at the slightest pain. The glass is left in place for half an hour, removing and replacing it once during this time. The same procedure is carried out each day until the end of the menstrual period. The hyperemia of the breast usually persists for some hours after the removal of the cup. This plan of treatment, according to Polano, not only relieves the dysmenorrhea, but also shortens the duration of the flow.

This plan of treating dysmenorrhea has not attained very wide adoption, and the few reports dealing with it would indicate that its results are certainly not very striking.

Measures for Permanent Relief of Dysmenorrhea.— The many plans of treatment which have in the past been advocated in the treatment of this troublesome symptom indicate that none has been eminently successful. This is especially true of primary dysmenorrhea, the treatment of which

still remains one of the important unsolved problems of gynecology. The fact that even hysterectomy has at times been resorted to, shows to what desperate straits gynecologists are sometimes driven in the management of such cases. The treatment of the two types of dysmenorrhea is quite different, and will be considered separately.

Measures for Permanent Cure of Primary Dysmenorrhea.— The physiological cure of primary dysmenorrhea is pregnancy. It is a well-known fact that this practically always marks the permanent disappearance of primary dysmenorrhea. Even when pregnancy does not take place, it is a common observation that marriage sometimes brings great relief from this symptom, probably because the relations of married life act as a stimulant to the development of the uterus. Unfortunately, marriage cannot always be prescribed with as much readiness as medicine. At any rate, the suffering and inconvenience of the patient are often so marked that measures looking for radical relief must be considered.

Importance of Accurate Diagnosis.— In all cases, it need scarcely be emphasized, it is of the greatest importance to assure oneself that the dysmenorrhea is actually of the primary type, i. e., that there is no pathological condition in the pelvis which may be responsible for the pain. This can often be ascertained only by careful examination under anesthesia. Whenever it is decided to anesthetize the patient for the purpose of such an examination, it is wise to prepare for dilatation of the cervix should no anatomic cause be found for the dysmenorrhea, so that the patient may be spared the inconvenience and risk of repeating the anesthetic.

Dilatation of Cervix by Rapid Method.— This still remains the most popular method of treating dysmenorrhea of the type now under discussion. This plan of treatment is of course based primarily upon the conception that dysmenorrhea is obstructive in origin. As has already been shown, however, there can be little doubt of the fallacy of this theory. On the other hand, there can be no question that dilatation of the cervical canal is often followed by relief from dysmenorrhea, sometimes permanent, more often temporary.

In former years, dilatation was usually accompanied by curettage of the uterus. In the majority of cases, however, there is no real indication for the curettage, and nothing is gained by its performance. Microscopic examination of the endometrium from such cases practically always reveals a normal structure.

Holden has analyzed the reports received from 95 patients at periods varying from one to twelve years after dilatation and curettage for dysmenorrhea. He finds that 40 per cent were entirely or very greatly relieved for at least one year, with 7 per cent of this 40 per cent having a recurrence after one year or more; 30 per cent had no relief at all, while the remaining 30 per cent had but slight relief or relief for a few months only. Marked maldevelopment of the pelvic organs was present in 20 cases, and in only 25 per cent of these were the patients relieved.

From a study of the clinical character of the pain experienced by the patients in these cases, Holden concludes that the prognosis for relief by dilatation and curettage is better when the pains are sharp and spasmodic. It is bad when the pains are dull. The statistics of Norris and Barnard give about the same results as those of Holden.

A description of the technic of the operation of rapid dilatation of the cervical canal is not within the scope of the present work. It may be found in any of the works dealing with operative gynecology. It should be emphasized, however, that the dilatation should be as thorough as possible in order to insure good results. Even then, unfortunately, there may be no relief from the menstrual pain. In other cases, as the above statistics indicate, the relief is temporary, so that it is frequently necessary to repeat the procedure. Since it seems to have been demonstrated that the mere widening of the cervical canal cannot explain the relief of the pain, it is probable that the good results of the operation in many instances are due to its stimulating effect upon the development of the uterus.

Continuous Dilatation by Stem Pessaries.— In order that dilatation of the cervix may be maintained more or less continuously, the use of various forms of stem pessaries is advocated by some. This measure is employed usually as a supplement to an initial rapid dilatation of the canal. Carstens, who has been especially enthusiastic concerning the value of the stem pessary, explains its good effect by its irritant action on the uterus, causing contraction and thereby giving the uterine muscle exercise, and causing it to develop like other muscles which are properly exercised. In other words, the pessary acts as a foreign body, causing efforts on the part of the uterus to expel it. The pessary used by Carstens is the Chambers pessary.

Even more popular than the latter has been the use of the Wylie drain. This is a bulbous stem with a lateral drain, which permits of free drainage of the uterine cavity. The pessary is introduced into the uterus, following a thorough dilatation of the cervical canal. This should, by preference, be performed about a week before the onset of a menstrual period. It is usually advisable to pack the vagina lightly after introducing the pessary into the uterus, so as to keep it from falling out immediately after the dilatation, when the cervix is of course very wide. It is even better to suture the pessary to the cervix with silk of silkworm gut. The patient should be kept in bed for a day or two. The instrument may be left in for a period of usually two months.

The principal objection which has been urged against the use of the stem pessary is the fact that it may cause a troublesome endocervicitis and perhaps actual ulceration. I have seen cervical infection as a result of the stem pessary. It is also stated that the drainage groove in the pessary may be blocked up, so that the pessary acts as a plug rather than as a drain.

While these objections are, to my mind, well founded, it is only fair to say that these complications appear to be far less frequent than one might expect. Moreover, those who have used the stem pessary extensively are

as a rule enthusiastic concerning this plan of treatment. Beyea, for example, reports that 22 of 26 single women in whom the Wylie drain had been used had been entirely relieved of menstrual pain, 2 were benefited but still had considerable pain, and 2 received no benefit. In the same way, 12 of 15 married women were relieved and 3 received no benefit. Of the 15 married women, 5 became pregnant after operation, 3 going to full term.

Plastic Operations on Cervix.— A number of surgical procedures have been recommended and practiced for the relief of dysmenorrhea, on the assumption that it is due to cervical stenosis. The principal operations of this class are those devised by Dudley and Pozzi. The first of these, which is practically the same as that suggested by Sims, consists in splitting up the posterior lip of the cervix as far as the internal os, and then suturing the mucosa of the cervical canal to that covering the pars vaginalis.

The operation of Pozzi consists in first making an incision laterally outward from the cervical canal through the cervical walls. A triangular piece is then resected from the centre of each of the four raw surfaces made by the two incisions. The mucosa of the lumen is then sutured to that of the outer surface of the cervix, thus covering the four raw surfaces and leaving the lumen of the cervical canal widely gaping.

Aside from the fact that these operations are based upon a faulty conception of the etiology of the dysmenorrhea, such procedures are open to the objection that they may increase the difficulty of labor in the event that pregnancy should later occur. My own limited experience with such operations has not made me very enthusiastic in their employment. In fact, I have abandoned their use. While favorable results are reported by a number of observers, there is little prospect that these operative procedures will ever become any more popular than they now are.

The Permanent Cure of Secondary Dysmenorrhea.— The permanent relief of this form of dysmenorrhea is of course dependent upon the removal or correction of the pelvic disease which is causing it. In some cases the removal of a myoma, an ovarian cyst, or a pyosalpinx may be necessary; in others, the correction of a retrodisplacement; and so on. The technic of the various operations which may be necessary for the relief of secondary dysmenorrhea is discussed in the various text books of operative gynecology.

MEMBRANOUS DYSMENORRHEA

General Considerations.— There is a form of dysmenorrhea, usually severe and cramp-like, in which the patient passes large or small pieces of membrane with the menstrual discharge. To this form the designation of membranous dysmenorrhea is given. The first description of the condition is usually credited to Morgagni, who reported a case in his " De Sedibus et Causis Morborum " (1779). The name of membranous dysmenorrhea was bestowed upon the condition by Oldham, who in 1849 contributed an interesting description of the disorder.

There was much discussion in former years as to the actual existence of such a condition as membranous dysmenorrhea. For example, Hausman, in an exhaustive consideration of the subject delivered before the Obstetrical Society of Berlin, arrived at the following conclusions: (1) A decidual menstrual disease of the uterine mucosa as a "morbus sui generis" does not exist; (2) all cases reported as decidual affections are to be considered as miscarriages in the first weeks of pregnancy, probably caused by some morbid condition of the ovum; (3) the coincidence at the time of menstruation is incidental; (4) a symptomatic treatment and abstinence from coitus for a few months is sufficient to cure the affection.

A considerable number of cases have been reported, however, in which the possibility of pregnancy can be absolutely excluded. This fact, together with the recent advances in the study of the menstrual histology of the endometrium, leaves no room for doubt as to the occurrence of membranous dysmenorrhea as a definite clinical entity.

Clinical Characteristics.— The distinguishing feature of this form of dysmenorrhea, as already mentioned, is the passage by the patient of a greater or less amount of membrane with the menstrual discharge. The membrane may be passed on the first day of the flow, but much more frequently comes away on the second or third, and occasionally even later. Before this happens, the patient usually suffers with severe cramp-like pains, usually compared in their intermittence with labor pains. After the membrane is passed, the pain almost always ceases. It is stated that the menstrual flow also becomes much more profuse, but I have not noted this in the cases which I have observed. Occasionally, as in Ehrenfest's case, membranes are passed at the menstrual periods without any pain whatsoever. These cases are, however, certainly not the rule, and when they do occur the designation of membranous dysmenorrhea is of course a misnomer.

Other than the occurrence of the pain, menstruation in most cases is quite regular and normal. Not infrequently there may be some pelvic lesion which causes more or less intermenstrual pain or other symptoms, but membranous dysmenorrhea is frequently observed when the patient is otherwise in good health.

Etiology.— Up to a few years ago the subject of the etiology of membranous dysmenorrhea was very obscure indeed. The work of Hitschmann and Adler, however, has given a new trend to investigation along this line, and has added substantially to our knowledge of the real nature of this condition. The older theories were, in the main, quite speculative in character. Scanzoni considered the affection as one of the congestive dysmenorrheas, explaining the painful expulsion of membrane by the fact that the blood, being prevented from escaping by the greatly thickened mucosa, gradually loosens the latter and causes its expulsion. Hegar and Eigenbrodt designate the affection as "dysmenorrhea apoplectica," while Gautier speaks of it as "uterine ichthyosis."

Up to quite recent years there were many who believed that membranous

dysmenorrhea is always the result of an inflammatory process, hence the name "exfoliative endometritis." Aschheim, after the examination of seven cases of menstrual membrane thrown off by patients observed in his clinic, states that such membranes are the product of an acute exudative endometritis. In general, he says, the membrane consists of necrotic stroma, filled with leucocytes, with a fibrinous reticulum. The membrane forms in the intermenstrual period, and is thrown off about the third day of menstruation. Remains of the uterine mucosa are usually to be found in the membrane, which Aschheim thus considers practically an inflammatory exudate. No bacteria were found in the membrane by Aschheim. The causes of the inflammation he describes as general and local. General conditions that cause exfoliation are anemia, chlorosis, scrofula, tuberculosis and syphilis. Local conditions are fibroma, chronic metritis, ovarian diseases, parametritis, abortion and stenosis of the canal of the uterus.

The recent work of Hitschmann and Adler discredits the theory of the inflammatory origin of membranous dysmenorrhea. These investigators described the cycle of histological changes which occur in the endometrium in connection with the menstrual cycle (Chapter IV), and, among other things, they demonstrated that in the premenstrual endometrium, as in young decidua, two definite layers can be differentiated. The superficial or compact layer is, on section, found to be comparatively poor in gland lumina, and to contain a large amount of stroma. The cells of the latter, it will be recalled, often exhibit much hypertrophy, so that they even suggest decidual cells in appearance. The deep or spongy layer is much richer in gland elements and contains much less stroma than the superficial stratum.

Hitschmann and Adler believe that the separation of a menstrual cast in membranous dysmenorrhea represents an exaggeration of the normal process. In other words, they consider that it is normal for more or less breaking-down of the uterine mucosa to occur at each menstrual period, and for fragments to be cast off with the menstrual blood. This is contrary to the opinion which has been held by many able investigators. On the other hand, many of the older writers, and some modern authors, have held the opinion which finds expression in the work of Hitschmann and Adler. The latter believe that in the most marked cases there is a complete separation of the superficial from the compact layer, with the formation of a complete uterine cast. When the process is less complete, larger or smaller fragments may be extruded from the uterus.

Mechanism of Detachment of Membrane.— Hitschmann and Adler believe that the cause of the separation of the membranes in these cases lies in the occurrence of unusually severe uterine contractions, which are especially likely to bring about this effect if the two layers of the endometrium are sharply differentiated from each other. According to their theory, the cause of the exaggerated uterine contractions in these cases is to be sought in an obstruction of the cervical canal by a clot of blood. Against this, as Ehrenfest points out, is the fact that dilatation of the cervix yields very

discouraging results in the treatment of membranous dysmenorrhea. There is no convincing evidence to support the explanation of Hitschmann and Adler, which must therefore be looked upon as a mere hypothesis.

Another view, which, however, is equally hypothetical, is that of Ehrenfest, who suggests that the thin septa between the glands of the spongy layer may, under certain conditions, be extensively destroyed. The factors which he mentions as possible causes of such destruction are interstitial hemorrhage and excessive compression from secretions retained in the glands. If blood vessels are ruptured by the destruction of the interglandular septa a submucous hematoma may form and bring about detachment of the membrane. The idea that the membrane is thus dissected away by submucous hemorrhage was suggested many years ago by Gottschalk and others.

Fig. 34.—Cast of Uterus in a Case of Membranous Dysmenorrhea (Dudley).

Structure of Menstrual Membranes.—Macroscopic Appearance.—A perfect menstrual cast of course possesses the shape of the uterine cavity. It presents three openings, two corresponding to the uterine ostia of the tubes, and one corresponding to the internal os (Fig. 34). Its internal surface is smooth, while externally it is irregular and perhaps quite shaggy. Its walls are usually thin and often translucent. In other cases, however, the walls are much thicker. Usually the membrane is more or less rolled up when it is discharged, so that its characteristic shape is not readily apparent. By floating it in water, however, its character and shape are revealed. Much more frequently the membrane is passed, not as a complete cast, but in the form of fragments of variable size and shape. Often they

are rather flake-like in appearance, and a number may be passed at one time.

Microscopic Structure.— From the viewpoint of the microscopic structure, two varieties of menstrual membranes may be distinguished: (1) the fibrinous, and (2) the endometrial.

(1) Fibrinous membranes. These, as the name indicates, are made up essentially of fibrin or clotted blood. The mechanism of uterine casts of this type is easy to comprehend. Under certain conditions, as yet little understood, menstrual blood coagulates within the uterine cavity, and the clot may be extruded as a mould of the uterine cavity. Cases of this type, to my mind, are not to be classified as instances of membranous dysmenorrhea. In a certain number, however, the meshwork of fibrin contains, in addition to leukocytes and red corpuscles, a considerable number of stromal cells. Usually the latter are large and swollen, and perhaps suggestive of decidual cells. When these tissue elements are present in considerable amount, the designation of membranous dysmenorrhea would seem to be justified.

(2) Endometrial membranes. Bell divides membranes of this type into two varieties, the thick and the thin. These terms, however, have reference to the thickness of the wall of the cast, and there would seem to be no especial advantage in making the distinction. The membranes which I have had the opportunity of examining microscopically have rarely been rich in glandular elements. When glands are observed they are usually rather wide and only moderately convoluted, if at all. In other words, they suggest, as they obviously are, the gland channels of the superficial layer of the endometrium.

The most conspicuous histological element in all these cases is the stroma. I agree with Bell as to the incorrectness of Cuthbert Lockyer's statement that "the cells in menstrual endometrial casts are small, shrunken, and branching; the stroma is formed of a slender adenoid reticulum." As Bell remarks, this description applies to the stroma in the postmenstrual or resting stages of the menstrual cycle. On the contrary, the stromal cells found in the endometrial cast are characteristically large and overgrown, this being accentuated by the edema which is almost invariably associated, and which gives the tissue a very loose texture (Fig 35).

The decidua-like appearance ("decidua-ähnlichkeit") sometimes observed in the normal endometrium just before menstruation is always exaggerated in the menstrual cast, although there are great differences in the degree of this change. In the most extreme cases the mimicry of genuine decidual cells is very striking, so that one finds it difficult to convince oneself that pregnancy has not been present. Bell lays stress on the "ground glass appearance" of the stroma caused by the marked effusion of blood serum among the cells. This, he says is absent in the decidua of pregnancy.

Diagnosis.— The conditions from which membranous dysmenorrhea must be distinguished are those which are likewise associated with the pas-

sage of membrane per vaginam. By far the most important of these is *early abortion*. The differential diagnosis between membranous dysmenorrhea and early abortion is frequently of great practical importance, and it is often exceedingly difficult, even with the aid of the microscope. As stated above, it was formerly believed by many that all cases of supposed membranous dysmenorrhea are really instances of early abortion. While this can no longer be accepted as true, it cannot be doubted that many cases are diagnosed as membranous dysmenorrhea which are probably early abortion, and vice versa.

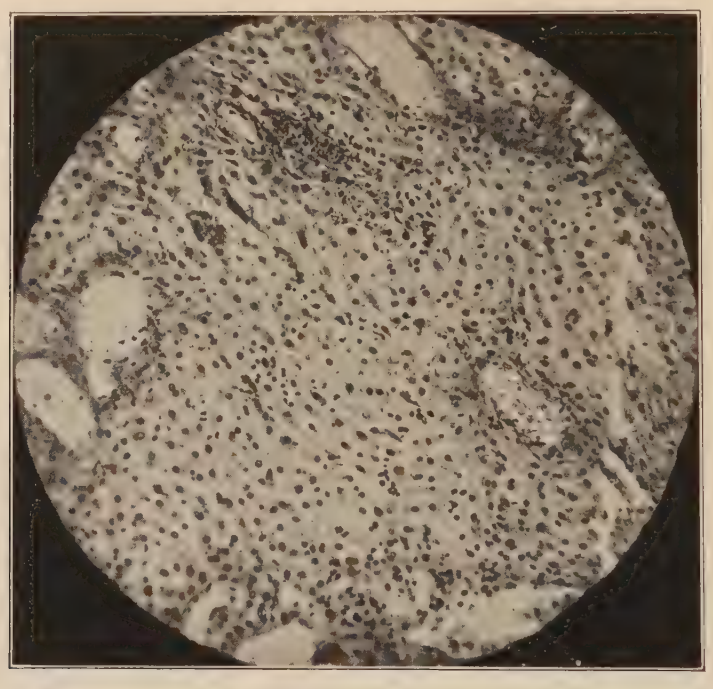

FIG. 35.— STRUCTURE OF UTERINE CAST OF THE DECIDUAL TYPE, ASSOCIATED WITH MEMBRANOUS DYSMENORRHEA.

The patient passed large flakes of membrane of this structure at each menstrual period (personal case).

Occasionally the history of the case is such as to make it reasonably or perhaps absolutely certain that pregnancy could not have existed. It is scarcely necessary to emphasize the caution which must be exercised in arriving at this conclusion. A case reported by Fieux illustrates this point. His patient was a woman who had always had extreme pain at the menstrual periods, at which time she had as a rule passed distinct membranous shreds. After a period of amenorrhea lasting two months, she had a painful but scanty menstruation, and one month later another painful period with the expulsion of membrane. Careful examination showed that the membrane contained a very small amniotic sac with a broken down embryo under ten

millimetres in length. The decidua had evidently been retained long after the death of the fetus.

From a microscopic standpoint, it is sometimes very easy to determine the exact nature of membranes passed at the menstrual period; at other times it is impossible. The presence of chorionic villi of course fixes the diagnosis of pregnancy. When these are absent, the diagnosis is not always easy. If the membrane consists of fibrin, with small, i. e., non-hypertrophic, stromal cells, pregnancy may be excluded with reasonable certainty. When, however, the membrane is made up of large decidua-like cells, as it so frequently is, the distinction between a menstrual membrane and early abortion may be exceedingly difficult. In these cases the history of the patient should be investigated with the greatest detail. Even then, only a presumptive diagnosis can be made in a certain proportion of the cases.

Vaginal membranes are occasionally passed during menstruation, and may be mistaken for those coming from the uterine body. In the majority of such cases the history will show that the patient has been using an irritant douche, or has perhaps been given treatment by a gynecologist. Silver nitrate especially is apt to cause the desquamation of thin membranous shreds from the vagina or from the pars vaginalis. If there is any doubt about the source of the membrane, the presence or absence of squamous epithelium on microscopic examination will decide the matter.

In certain other conditions, as in *adenocarcinoma of the fundus,* or with a *sloughing submucous myoma,* it is possible that the patient may in rare cases pass shreds of tissue with the menses. The other signs and symptoms of such conditions are usually so definite that the question of differentiating them from membranous dysmenorrhea almost never arises.

Prognosis.— The prognosis of membranous dysmenorrhea is as a rule distinctly unfavorable. In some cases there are periods of remission from both the pain and the passage of membranes, but relapses are the rule.

Treatment.— On the whole, the treatment of membranous dysmenorrhea cannot be said to offer any great prospect of success. Aside from the mere relief of pain, the measures which have been recommended are quite empirical. Two plans of management have been practiced in the past. The first, on the assumption that the condition is due to some local inflammatory process in the uterus, consists in intra-uterine applications of such substances as carbolic acid, iodin, or even sulphuric and nitric acids. In addition to this local medication, curettage has often been resorted to, sometimes repeatedly.

The other plan of management embodies the principle of "masterly inactivity," so far as local treatment of the uterus is concerned. According to this plan, only general treatment is carried out, by means of such tonics as iron and arsenic. A neurotic tendency is said to be present in some cases, and for this various nerve sedatives, such as the bromids, are administered.

From a negative point of view, at least, the latter method of treatment would seem to commend itself. Certainly there is no real evidence that

local antiseptic or escharotic treatment of the uterine mucosa has ever been of any service. If our present day conception of the nature of membranous dysmenorrhea be correct, such drastic treatment is irrational, to say the least.

For the symptomatic treatment of the pain associated with this condition the various measures which have already been recommended for the relief of dysmenorrhea are of service.

NASAL DYSMENORRHEA

General Considerations.— A form of dysmenorrhea of rather special etiology and also, I may say, of rather special interest, is that to which the rhinologist Fliess called attention in 1893, and on which he published an extensive monograph in 1897. I refer to the so-called "nasal dysmenorrhea," which has, since its description by Fliess, been the subject of sporadic reports by various authors. It seems to me, however, that it has not been investigated with the thoroughness or finality to which its interest and importance would seem to entitle it. It has long been known that there is a biological and perhaps also a physiological connection between the reproductive organs and the nose. Siefert, writing in 1912, gives reference to as many as 296 articles dealing with this relationship which are to be found in the literature.

The "Genital Spots" in the Nose.— From an anatomic standpoint it is of interest to note that erectile tissue is found in the nose, as in the genital tract. In the nose the erectile tissue is found especially at the anterior end of the inferior turbinated bone and in the small circumscribed area known as the tuberculum of the nose. These are the two areas which Fliess designated as the *genitalstellen* or *genital spots*. During menstruation these spots, according to Fliess, are invariably swollen and congested, so that they bleed on the slightest touch. In addition, they are said to be markedly hypersensitive during the menstrual flow. All of these characteristics are said to disappear as soon as menstruation ceases. The theory that there is some intimate relationship between these spots and the functions of the generative organs is further strengthened by the frequent occurrence of nasal bleeding as a vicarious phenomenon at the menstrual epochs.

Theories of Nature of Relation Between Generative Organs and Nose.— No very satisfactory explanation has been presented for the evident relation which exists between the olfactory and sexual apparatus. It has been suggested that the physiological connection between the two is brought about through the agency of the sympathetic nervous system. Siegmund, on the other hand, attempted to explain it by a rather complicated theory based upon the so-called hypothesis of Head. In view, however, of the great advances which recent years have brought in our knowledge of the internal secretions, and knowing as we now do that these internal secretions or hormones are capable of exerting a selective action upon organs or tissues far removed from those which produce the hormones, it seems much more logical to look to the hormone theory for an explanation of the many

interesting evidences of a functional relationship between the nose and the sexual organs.

The Cocain Test of Nasal Dysmenorrhea.— Fliess distinguishes two clinical types of menstrual pain, one in which the pain ceases with the appearance of the menses, the other in which the pain continues after the menses have commenced. The first, he believes, is always due to cervical stenosis. The second type includes many patients in whom cocainization of the genital spots causes cessation of the menstrual pain. These are the cases which Fliess designates as "dysmenorrhea nasalis." The condition of the pelvic organs he says is without importance, being normal in some and pathological in others.

Permanent Cure of Nasal Dysmenorrhea.— If, in cases of this type, the cocain test proves positive and the patient obtains temporary benefit, it is then often possible to give her permanent relief by cauterization of the genital areas by means of the galvanocautery, electrolysis, or trichloracetic acid. In addition, any pathological condition existing in the nasal chambers must be remedied. More than 100 cases in which permanent cure of dysmenorrhea followed this method of treatment are offered by Fliess in substantiation of the views above expressed.

A number of other observers have published results in confirmation of the claims of Fliess. Among these is Schiff, whose work was done in the clinic of Chrobak, at Vienna. Not only does Schiff endorse the findings of Fliess, but he goes so far as to assert that the application of cocain to the anterior end of the inferior turbinate causes a disappearance of pain in the hypochondrium, while a similar application to the tuberculum of the septum controls the backache. On the other hand, irritation of these spots with the end of a probe produces the corresponding pain. In other words, the hypochondriac pain seems in some way to be related with the anterior end of the inferior, and backache with the tuberculum. I am not aware of any observations in confirmation of this hypothesis, which moreover lacks the ring of plausibility, in view of the different mechanism of these various types of pain in different cases. Schiff, I may add, found that 72 per cent of all cases of dysmenorrhea could be treated by the nasal method.

A similar experience is reported by Linder from Amann's clinic at Münich. About thirty cases were treated by Fliess' method. Almost every patient was relieved. Incidently, he remarks that several patients were completely relieved when water was substituted for the cocain without their knowledge, suggesting the importance of the psychic factor in the treatment. In others only cocain afforded relief. He believes that suggestion plays an important part in the cure of such cases, but does not believe that it explains all the good results.

The recent publications of Mayer and Brettauer have brought this subject to the attention of the profession of this country. Brettauer in 1913 reported 66 cases treated by the nasal method. Of these, 33 were immediately benefited, by which Brettauer means that the first menstruation after the

treatment was painless; 17 were immediately improved, the degree of pain being much less; 15 showed no relief whatever. Taking into consideration the cases which he was able to follow up, he finds that in more than one half of those treated there was immediate relief, and that relief was permanent in about one third. He is therefore convinced of the value of the treatment.

Equally enthusiastic is the opinion of Mayer, who has recently reported a series of 93 cases, which number, I believe, includes those of Brettauer. The majority of Mayer's patients are described as having had premenstrual headaches and nausea from one to two weeks before the period, to be followed by abdominal pains during the first two days, often of so severe a nature as to compel the patient to go to bed, losing at least two days each month.

As to the effects of the treatment he says "When we recall the extreme pallor of one of these sufferers as she slowly dragged her way to the office for treatment, her firmly compressed lips and utter weariness, and then within a few minutes after a local application to her nose how her color came back, her breathing was free and she went about her duties instead of to bed as usual, we feel that we have earned her gratitude." Of his 93 patients, no report was available from 12, leaving 81 for analysis. Of these 48 were cured, 14 were improved, and 19 were unrelieved. He concludes that permanent relief is obtainable by intranasal treatment in from 50 to 75 per cent of the cases.

Need of Caution in Estimating Results of Treatment.— Kuttner agrees as to the frequency with which dysmenorrhea disappears after cocainization of the genital spots. He finds, however, that applications of menthol and other substances will produce the same effect. He believes that the good results of the nasal treatment of dysmenorrhea are due in a large measure to the psychic influence on the patient, the general effect of the cocain after absorption into the circulation, and the improvement in the patient's general condition which comes when the nasal treatment, as often happens, brings about cure of a nasal stenosis.

To illustrate the risk of jumping at conclusions as to the success of the treatment, he mentions the case of a patient who had for five years been treated regularly for four or five days each month in his clinic. Without the treatment the pain would be unbearable. This case, he says, would naturally be looked upon as a good demonstration of the intranasal treatment, were it not for the fact that on Sundays and holidays, when the clinic was closed, the patient was in the habit of taking a few drops of cocain solution by mouth, with the same relief as when it was applied in the nose.

Method of Treatment.— It is advised by Mayer and Brettauer that the local treatment in the nose be given four times, at intervals between the menstrual periods. As already stated, the application of a twenty per cent cocain solution is used for the "cocain test," to distinguish cases of nasal dysmenorrhea from others. If the test be positive, more permanent relief

will be given by treating the genital spots at intervals, as above mentioned, with trichloracetic acid.

The areas to be treated are first anesthetized by applying for a few minutes pledgets of cotton saturated with a 20 per cent solution of cocain. When sensation has disappeared, a crystal of trichloracetic acid is applied on the end of a probe to the tuberculum septi, and another in the same way to the other genital spot at the anterior end of the inferior turbinate. The procedure is carried out in both nasal cavities. The application is followed by the formation of a slough, which disappears in about five days, when the treatment may be repeated, thus allowing of about four treatments between menstrual periods.

If the ensuing menstrual flow is unaccompanied by pain, no further treatment may be necessary. If, on the other hand, dysmenorrhea still continues, the same plan of treatment must be repeated a second time. The galvanocautery has been used in some cases instead of the trichloracetic acid, but its employment is accompanied by some danger of synechia.

XX

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CHAPTER XXI

INTERMENSTRUAL PAIN

Definition.— In 1872 Sir William O. Priestly described the condition to which he gave the name of intermenstrual pain. The special characteristic of the disorder is the regular recurrence of pain at some definite period in the intermenstrual cycle, usually about midway between two menstrual periods. By the Germans the condition is spoken of as "mittelschmerz." As Kelly points out, however, this term is not a very accurate one, inasmuch as the pain does not always occur at the middle of the intermenstrual period.

Frequency.— The total number of cases reported in the literature is not very large, but all those who have written on the subject insist that the condition is by no means as rare as is generally believed. According to Rosner, the condition was encountered 12 times among 2350 gynecological patients. Theilhaber also emphasizes the fact that careful inquiry into the history will place in this category many cases which would otherwise pass unrecognized. He states that by such intensive search he came upon 12 cases in one year of his polyclinic practice. In spite of these observations, my own feeling is that the disorder must be looked upon as relatively uncommon. It must be borne in mind that the diagnosis of intermenstrual pain is not justified unless the pain recurs regularly at fixed intervals for at least a number of months. Either the patient must be observed over a long period of time, or else her history on this point must be unimpeachable. Although I have long been interested in the study of menstrual disorders, I have encountered only a very small number of definite cases of intermenstrual pain.

Time of Occurrence of Attacks.— In the great majority of cases, the pain occurs at or near the middle of the intermenstrual epoch, extending over into the second half of the latter. Unfortunately, in many of the reported cases, the exact date of occurrence of the pain with reference to the menstrual periods is not given. Often, however, instead of coming exactly midway between periods, the attacks will occur either earlier or later in the cycle. The essential feature is its periodicity, which is often so well marked that, to quote Kelly, "the date of the approaching period can be foretold from the day upon which the intermenstrual pain appeared." To illustrate this, Kelly gives the following record of a typical case of his own.

Menstruation	December	1		
Intermenstrual pain	"	10	Interval	9 days
Menstruation	"	19	"	9 "
Intermenstrual pain	"	30	"	11 "
Menstruation	January	10	"	11 "
Intermenstrual pain	"	21	"	11 "
Menstruation	February	1	"	11 "
Intermenstrual pain	"	17	"	16 "
Menstruation	March	5	"	16 "

It is interesting, as well as significant, to note that during periods of amenorrhea, as during pregnancy or lactation, there is a cessation of the attacks of intermenstrual pain.

Character of the Pain.— Many adjectives have been employed in the description of the character of intermenstrual pain by those who have reported cases. It is variously described as "sharp," "paroxysmal," "dull," "aching," "neuralgic like," etc. In other words, no especial type of pain would seem to be characteristic of this condition.

Location of Pain.— As a rule the pain is referred chiefly to one or other of the iliac fossae — sometimes both. In severe cases the pain is apt to become general over the entire lower abdomen, and is often associated with backache. Not infrequently it radiates down one or both legs.

Duration of Pain.— In mild cases the pain lasts for only a few hours, but in others, the duration may be several days, or even up to the onset of the next menstrual period. Most frequently the pain is somewhat intermittent, periods of relief interrupting its severity.

Associated Vaginal Discharge.— In a large number of the reported cases — about one half — intermenstrual pain is associated with a vaginal discharge. As a rule this is described as being mucoid or watery, but it may be thick and yellowish. A patient whom I recently saw in consultation with Dr. W. J. Schmitz, of Baltimore, stated that each attack of pain was accompanied by a dark brownish discharge. In some cases the discharge occurs just before the onset of the pain, while in perhaps the larger number its occurrence and subsidence are coincident with that of the pain. Exceptionally the discharge may be slightly bloody, although, as Kelly cautions, this may be due to such associated conditions as polypi, endometritis, etc.

Age of the Patients.— As a rule intermenstrual pain does not begin with the inauguration of menstrual life, this occurring in only three of forty-one cases collected by Kelly. "In ten cases (including the three beginning with first menstruation) the patient was under twenty when the pain began; twenty-nine of the remaining cases were between twenty and thirty-five; while two were over thirty-five." Heaney's figures, based on sixty-six collected cases, refer to the age of the patients when they came under observation and not to the age of onset of the trouble. He found that 42 patients were between the ages of 25 and 35, ten over 35 years, nine under 25 years, while in 5 the age was not stated. These figures cor-

roborate those of Kelly, and confirm the latter's statement that the affection is one which belongs to the period of full sexual activity.

Marital and Obstetrical Histories of Patients.— Both Kelly and Heaney emphasize the frequency with which sterility is observed in women subject to intermenstrual pain. Of the former's 64 cases, "32 had never had children or miscarriages (eleven of them being married and 21 single). Thirteen had had neither children nor miscarriages for as much as 5 years, and in most cases much longer. Fourteen had had children, or miscarriages, or both, within 5 years; and the condition of 5 as regards child bearing was not stated." Heany, again, found that among 35 who were married, 11 had never been pregnant, while 11 had been pregnant once, 7 twice, 4 three times, 1 four times, and 1 nine times. In one of my own cases, the trouble dated definitely from a miscarriage nine months previously, the patient having before this enjoyed good health.

Character of Menstruation.— There is nothing characteristic in the menstrual histories of patients who exhibit intermenstrual pain. Very often menstruation is associated with dysmenorrhea, although this is almost always described as much less severe than the intermenstrual pain. As far as the periodicity and amount of the flow are concerned, there would seem to be no especial influence, variations in this regard being attributable to accompanying pelvic lesions of one form or another.

Associated Pelvic Lesions.— In perhaps the majority of cases intermenstrual pain occurs in women who suffer with some form or other of pelvic disease. Often the lesion is of trivial nature, while at other times it is of much greater significance. Frequently no abnormality is discoverable in the pelvis, even on the most careful examination. Even when pelvic lesions are found, moreover, a causative rôle cannot be attributed to them, especially in view of the fact that the location of the intermenstrual pain often bears no relation to that of the lesion.

Etiology.— Practically nothing of a definite nature is known concerning the etiology of this interesting disorder. Many theories have been advanced to explain it. Some of them are quite grotesque, and none of them can be accepted as proved. Among the palpably far fetched views may be mentioned that of Drennan, who believes the pain is due to the escape of the non-impregnated ovum through the cervical canal, thus causing painful expulsive contractions of the uterus. The majority of authors attribute the pain to one form or another of pathological change in the pelvic organs. Thus, Rosner is of the opinion that the cause is a chronic pelvic congestion, brought about by a vasomotor disturbance of ovarian origin. Fehling believes that there is always an associated chronic inflammatory process in the uterus and ovaries. Palmer considers the cause to be oöphoritis or perioöphoritis, which prevents the rupture of the graafian follicles. Addinsell looks upon profluent salpingitis as the cause in the 4 cases which he reports. Many other authors might be quoted who support the anatomic explanation of the condition.

The striking periodicity of the disorder makes it seem almost certain that it is of ovarian origin. The former view of the relation between menstruation and ovulation, which assumed that they occur synchronously, presented an obstacle to the hypothesis that ovulation might be the cause of intermenstrual pain. Heaney believes that the intermenstrual pain really represents an effort at menstruation, the type of which is thus changed from a four week to a two week interval. Our newer knowledge of the relation between menstruation and ovulation, as set forth in Chapter XVI, makes unnecessary these hypotheses. It is now quite generally accepted that ovulation does not occur at the menstrual period, but at a period varying probably from about the seventh to the fourteenth days of the menstrual cycle. In other words, intermenstrual pain is commonly observed at about the time of normal ovulation, which almost surely plays an important, perhaps an essential part, in its causation. Just what the abnormality of ovulation is that produces pain in these patients cannot be stated. Certainly normal ovulation is not associated with pain. After all, then, the question is still an open one, although I feel that the advances being made in our knowledge of the ovarian function will aid materially in the solution.

Treatment.— Since we know so little of the etiology of intermenstrual pain, it is not surprising that its treatment is far from satisfactory. In the first place, the cure of any important pelvic lesions, whether by operation or otherwise, is of importance, especially when they are causing other symptoms in addition to the intermenstrual pain. Other than this, the treatment consists principally in the relief of pain, just as in the treatment of an attack of dysmenorrhea. Rest in bed, together with hot applications to the seat of pain, is of importance. In the less severe cases, such drugs as aspirin or the various coal tar products may give the desired relief. In the more severe forms, codein or perhaps even morphin may be necessary to control the pain, although, it need not be said, such drugs should be handled with the greatest caution, in order to avoid habit formation.

To show the multiplicity of measures which have been used in the treatment of intermenstrual pain, I can do no better than to quote Kelly's summary of the results of treatment in the cases which he collected from the literature. He says "Of the various modes of treatment adopted, the results are as follows: Dilatation and curettage was tried in eleven cases, entirely without benefit, except in one instance where the uterus was steamed out after it, and in this case the intermenstrual pain had lasted but a few months. Ovarian, parotid, and thyroid extracts were given in one case without relief, but in another the thyroid alone was followed by complete recovery. Electricity over the ovarian region was tried in four cases, two of which were somewhat improved, while the other two derived no benefit whatever. Removal of one ovary and tube was tried in four cases where the localization of pain in the ovarian region seemed to indicate it. In one instance the pain was relieved for a period of eight years, and in

another it has now been absent for six; the other two cases were entirely unbenefited. The appendages were removed on both sides in five cases, two of which were among the cases mentioned where one ovary was first removed without benefit. The results in one instance are not definitely stated, although, judging from the context, they were good; of the other four cases, three were entirely relieved and the other not at all. In the latter instance, however, menstruation continued after the operation and it is to be supposed that some ovarian tissue remained behind. Suspension of the uterus was tried in three cases of retrodisplacement, with complete relief in one case, partial relief in another, and none at all in the third.

"Partial relief was also obtained in three cases from a course of baths or medicinal waters; in one case from absolute rest in bed during the attacks of pain, with straightening of the uterus, which was in extreme anteflexion; and in one case from the use of a Hodge pessary for extreme anteflexion, together with the relief of a coëxisting endometritis.

"Complete relief resulted in one case from the use of an intrauterine pessary for marked anteflexion; in two cases from a six months' treatment for endometritis, nature not stated; in one case from the cure of an eroded cervix; and in one from rest in bed during the attacks, with support of the uterus by tampons."

XXI

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CHAPTER XXII

UTERINE HEMORRHAGE

General Considerations.— The study of uterine bleeding is given a peculiar interest by the fact that the uterus is the only organ in the body from which a periodic hemorrhage occurs as a physiologic phenomenon. The logical point of departure in the investigation of pathologic uterine hemorrhage, therefore, would seem to be a study of the normal type of uterine bleeding, that is, menstruation. In the study of all the menstrual disorders the tendency has been to lose sight of the fact that there are many links in the menstrual chain, and to emphasize some one factor at the expense of others, which may be equally important. As regards the explanation of uterine bleeding, it is the anatomic point of view which has received most attention. This is not surprising when we consider that up to very recent times our knowledge of the menstrual process has been much more highly developed along anatomic than along physiologic lines, and that structural alterations in an organ are far easier to demonstrate than aberrations of function. More and more, however, we are beginning to realize that the uterus is only a keyboard on which many variations are played by a complicated menstrual mechanism, whose ramifications extend far beyond the confines of the pelvic cavity. Not only the uterus, but all the other constituent parts of the menstrual apparatus as well, are subject to disturbances of one form or another, and hence none of them should be overlooked in the investigation of uterine hemorrhage of obscure causation. The causes of *menorrhagia,* i. e., excessive bleeding at the menstrual periods, and of *metrorrhagia,* i. e., intermenstrual bleeding, may conveniently and properly be discussed together.

Relative Importance of Anatomic and Physiologic Factors.— At the outset it may be conceded that in the majority of instances the cause of uterine bleeding is anatomic, in some cases very frankly so. For example, uterine cancer is a perfectly obvious cause of bleeding from the uterus, just as rectal cancer may cause bleeding from the bowel. The same clear relationship is seen in the case of a few other lesions, more especially those of neoplastic type. We may thus distinguish, first of all, a type of uterine hemorrhage clearly due to well defined and easily demonstrable causes in one part or another of the uterus. There would be hemorrhages from lesions of this type, even though there were no such thing as menstruation to cause a periodic flareup in the pelvis.

A second group of cases may be distinguished in which a lesion of some

sort exists either in the uterus or in the adnexa, but in which hemorrhage would probably not occur, were it not for the extra congestion which each menstruation brings with it. A tubal inflammatory mass or an ovarian neoplasm might not in itself be capable of producing hemorrhage, but it frequently exaggerates the menstrual hyperemia, and hemorrhage is the result. When metrorrhagia or intermenstrual bleeding occurs, it would seem at first thought to indicate a direct effect of the lesion itself on the pelvic circulation. This, however, does not necessarily follow, for it is possible, as some have contended, that in many of these cases the disturbance of the menstrual mechanism is much more fundamental, involving the function of the ovary itself.

Finally, there is a third group of cases in which uterine hemorrhage occurs in the entire absence of any clearly demonstrable disease in any of the pelvic organs, and in which the explanation must be sought in some abnormality of function rather than of anatomic structure. Numerically speaking, cases of this type make up perhaps the smallest group, but they are of considerable importance nevertheless.

Classification of Causes of Uterine Bleeding.— It will be recalled (Chapter VII) that the factors concerned in menstruation are (1) an underlying cause, dependent upon the endocrin activity of the ovary, and influenced by other endocrin organs as well; (2) a nervous mechanism, essentially vasomotor in nature; and (3) the uterus, and especially the endometrium. In addition, the state of general health also exerts an influence upon the function of menstruation, as will be discussed in a later chapter (Chapter XXV). The important point to bear in mind is that uterine bleeding may be due to a disorder of any of the factors named, and that an intelligent study of a given case must embrace a search, not for anatomic alterations alone, but for deviations from the normal physiology as well. From this standpoint, the causes of uterine bleeding may be considered under the following heads: (1) General or constitutional; (2) Anatomic; (3) Fundamental or internal secretory; (4) Nervous.

CONSTITUTIONAL CAUSES OF UTERINE HEMORRHAGE

As in the case of other menstrual disturbances, uterine hemorrhage, especially menorrhagia, may at times be noted in connection with general diseases, even when the generative organs themselves are normal. Among the more important general conditions which may be influential in increasing the menstrual flow may be mentioned the following:

Acute Infectious Diseases.— Acute infectious diseases, such as typhoid fever, pneumonia, influenza, the exanthemata, etc. More frequently the tendency of these diseases is to inhibit or lessen the menstrual flow, but occasionally an opposite effect may be produced.

Constitutional Diseases.— Constitutional diseases, such as anemia, diabetes, syphilis, hemophilia, scurvy, etc. In the case of the first two,

menorrhagia seems to be less frequent than amenorrhea. In certain instances, however, the associated lowering of vitality appears to bring about an increased permeability of the blood vessels, which perhaps explains the menstrual excess.

Organic Diseases.— Organic diseases, such as pulmonary tuberculosis, hepatic cirrhosis, chronic valvular disease of the heart, and chronic nephritis, especially when associated with high blood pressure and other pronounced manifestations of cardiovascular disease.

Chronic Intoxications.— Chronic intoxications of various kinds are said to produce excessive menstruation in certain instances. Under this head would be placed chronic alcoholism, phosphorus poisoning, lead poisoning, etc.

The relation of general disease to uterine hemorrhage is discussed at greater length in Chapter XXV.

ANATOMIC CAUSES OF UTERINE HEMORRHAGE

Polypi.— These may spring from either the cervix or the body of the uterus. In either case they may be a source of uterine bleeding. The cervical polyp is often associated with endocervicitis. The bleeding to which it gives rise is usually independent of the menstrual cycle, i. e., it is more likely to be a metrorrhagia than a menorrhagia, though both are often noted. Such patients observe that coitus, long periods of standing, heavy lifting or other severe exertions are apt to be followed by the appearance of a bloody discharge, sometimes slight in amount, in other instances rather abundant. In some cases, especially of large cervical polypi, the menstrual flow itself is excessive.

Cervical Polypi.— Cervical polypi are often palpable on vaginal examination, as tit-like protrusions from the cervical canal. They are most frequently quite small, perhaps no larger than a small pea; often they are multiple. Their small size, together with their soft consistency and their movability, makes it easy to overlook them unless direct inspection is made of the cervix through a bivalve speculum. They can then be seen peeping out of the cervical canal a greater or less distance, depending on the length of the pedicle. The bright red color of the polyp is in sharp contrast to the dull opaque hue of the pars vaginalis. Occasionally cervical polypi become quite large.

The common cervical polyp is made up, histologically, of the same elements as the normal cervical tissue, of which it is only a heaping up. The glands are often more or less dilated, and are lined by the characteristic high, slender epithelium of the cervix. Normal cervical epithelium covers the surface of the polyp, although it is often lost through superficial ulceration. The covering epithelium is either columnar or stratified squamous, depending on the level from which the polyp springs. The stroma is edematous and rich in blood vessels. The vascularity of these little growths explains the bleeding which they produce.

Corporeal Polypi.— In the most extreme cases, the entire endometrium may be involved in a polypoid process, giving rise to the so-called polypoid or fungous endometritis, first described by Olshausen. We are here concerned, however, with the discrete polypoid growths which are often found springing from the endometrial surface, and which are a frequent source of uterine hemorrhage. In contrast to cervical polypi, they are more likely to cause menorrhagia than metrorrhagia. Not infrequently the hemorrhage is excessive, its frequent recurrence weakening the patient very decidedly. When the polyp is large and possesses a long pedicle, it pokes its way out through the cervical canal, so that its diagnosis becomes as simple as that of the cervical polyp. Unless this occurs, however, its recognition is not by any means so simple, being made possible only by curetting or perhaps even vaginal hysterotomy.

The polypi found in the body of the uterus are of two principal types, leaving aside those associated with malignant disease of the uterus. The majority are, as in the case of the cervix, merely localized poutings of the endometrium, from which they differ in only a minor way. Frequently they are rich in gland elements, so that they are often spoken of as glandular polypi. As in the case of cervical growths, the stroma usually shows edema and marked vascularity, with inflammatory infiltration near the surface of those in which secondary infection has occurred. The surface, where not destroyed by ulceration or sloughing, is lined by the short columnar epithelium of the corpus uteri, which is also, of course, continued into the gland depths.

Much more frequently than in the cervix, polypi of the corpus are myomatous in nature. This group will, however, be considered under another head.

Cervical Ectropion and Erosion.— A frequent result of cervical lacerations is a rolling out or eversion of the mucosa of the cervical canal, a condition sometimes erroneously spoken of as erosion. Endocervicitis is almost invariably the result, being characterized clinically by persistent leucorrhea. The engorgement of the everted cervical mucosa is sometimes the predisposing cause of slight bloody discharges after coitus, or possibly even after such exertion as that of lifting, etc. The same thing is true of the genuine erosion, which is far less frequent, and in which there is an actual destruction of the superficial tissues of the cervix. In the so-called papillary erosion, the mucosa is thrown up into many papillary elevations, covered by the columnar cervical epithelium.

Retention of Gestation Products.— Perhaps the most frequent cause of uterine hemorrhage is incomplete abortion. This is easy to understand when one considers the extreme frequency of abortion, both spontaneous and induced, and the likelihood of some of the products being retained. Sometimes the dead embryo itself remains in the uterus; more frequently it is the placenta or membranes.

Clinical Considerations.— In the very early cases the woman herself

may be unconscious of the fact that she has been pregnant and that she has aborted, the embryo being so tiny that it escapes detection. In these cases there is perhaps a delay of only a few days in the menstrual period, followed by a period of bleeding which often does not exceed the normal duration of menstruation, for which it is thus mistaken. Pain may be altogether absent. On the other hand, when pregnancy is more advanced, abortion is characterized by a greater or less amount of cramp-like pain and by the occurrence of free uterine bleeding.

As a rule the expulsion of the fetus is preceded by a more or less abundant bloody discharge, which may persist for many days, and perhaps for a number of weeks. If both fetus and placenta be expelled, the bleeding usually ceases rather promptly. On the other hand, if the placenta remains behind, bleeding may continue indefinitely. While in some cases it may be surprisingly slight, in others it is alarming, possibly exsanguinating the patient. In a certain number of instances portions of the placenta may be retained for long periods of time without causing any bleeding. In a recent case of my own, one of the placental cotyledons had been left behind in a case of full term delivery, causing no symptoms until seven weeks later. At this time there was a sudden profuse uterine hemorrhage, necessitating immediate emptying of the uterine cavity. The placental mass was molded to the interior of the uterus, constituting a typical placental polyp. The hemorrhage in such instances is obviously due to separation of the partially organized mass by the expulsive contractions of the uterus.

In a large percentage of cases, especially of the early group, the patient does not seek medical advice until long after the abortion has occurred. She may even, as already mentioned, be ignorant of having been pregnant. Hemorrhage may have continued for many weeks, either constantly or intermittently. In such cases the true nature of the intra-uterine condition can be recognized only by curetting. If the curette brings away the characteristic dark shreddy tissue which makes up the placental structure, the diagnosis is macroscopically obvious. Very often, however, the curetted tissue cannot be distinguished from thickened endometrium. In such instances the aid of the microscope must be invoked in making the diagnosis.

Histological Findings.— The histological elements which justify a diagnosis of a preëxisting pregnancy differ according to the stage at which the latter was terminated and the time which has elapsed since the occurrence of the abortion. Sometimes the *glands* of the endometrium show the *exaggerated hypertrophy and tortuosity* which characterize early pregnancy. On cross section the lumina are scalloped, the epithelium being low and of one cell thickness. The angles produced by the infolding of the glands may be covered by tuft-like epithelial masses several cells thick. This appearance is evidently due to the manner of section of these protruding angles. It should be emphasized that the presence of such markedly hypertrophic glands in uterine curettings is not in itself pathognomonic of pregnancy, for such a picture may be closely mimicked by an exaggerated

premenstrual reaction in the endometrium in the absence of pregnancy. On the other hand, this histological picture should always excite suspicion, and should always impel one to make a careful search for other elements which are more distinctive of pregnancy.

Another link in the chain of evidence is at times obtainable from the appearance of the stroma. Curettings removed postabortum commonly contain larger or smaller fields of *decidual cells*. The latter, as is well known, are merely the hypertrophied stromal cells of the endometrium.

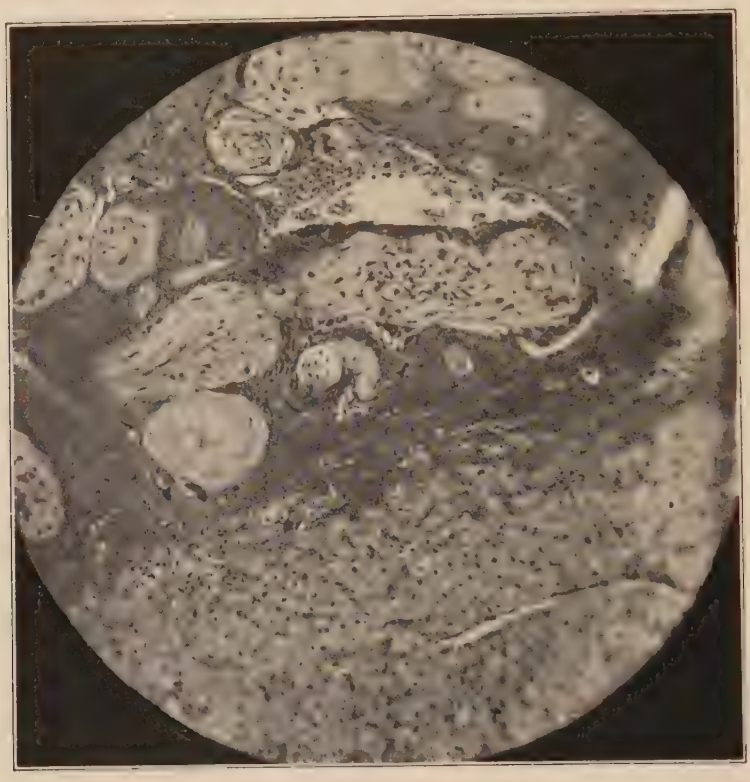

Fig. 36.— Curettings from a Case of Incomplete Abortion.

The upper half of the photograph shows a number of somewhat degenerated chorionic villi, while the lower portion is taken up by a broad field of decidual cells, presenting a mosaic-like appearance.

As in the case of the uterine glands, a moderate degree of hypertrophy is often noted in the stromal cells in the premenstrual period, giving them a decidua-like appearance (decidua-ähnliche zellen). When the cells are large and ovoid, with a broad zone of protoplasm surrounding the nucleus, so that they resemble cartilage cells, the diagnosis of a preceding pregnancy is reasonably certain. In outspoken cases the decidual cells occur in broad fields of mosaic appearance. (Fig. 36.) In cases in which considerable time has elapsed since the abortion they may occur only in patches here and

there. They often form thick mantles around the endometrial blood vessels, which, furthermore, not infrequently exhibit marked endothelial proliferation or a rather characteristic perivascular "fibrinoid" appearance.

The most distinctive element in the diagnosis, and the only one which, theoretically at least, is absolutely pathognomonic of pregnancy, is the presence of *chorionic villi*. (Fig. 36.) Being a part of the embryo itself, their diagnostic value is absolute. Except when the abortion has been very recent, the villi are more or less degenerated. Indeed, in many instances only their outline is discernible — the so-called "shadow villi" or "ghost villi." In a large proportion of cases, to be sure, chorionic villi are not found at all. In these, however, the presence of one or more of the elements above described, i. e., characteristic decidual cells, pregnancy glands, blood vessel changes, etc., makes the diagnosis quite certain. It may be added that with the pregnancy pictures in the endometrium there is often combined that of chronic endometritis, with round cell infiltration of the stroma. In the more recent cases, polymorphonuclear leukocytes are present in abundance.

Endometritis.— Up to the time of our newer knowledge of endometrial histology, i. e., up to the time of the investigations of Hitschmann and Adler, in 1908, chronic endometritis was quite generally looked upon as an extremely frequent disease. It was, furthermore, held responsible for many cases of uterine hemorrhage, as well as of leukorrhea. We know now, however, that chronic endometritis is a relatively infrequent condition. For example, only 48 instances were found by Cullen in an examination of 1800 curettings. The gland changes upon which the diagnosis of chronic endometritis was formerly based we now know are purely physiological in character.

Not only is chronic endometritis uncommon, but it is not easy to understand how it can produce uterine bleeding even when it does occur. The thickening of the endometrium and the preponderance of interstitial tissue in it might even lead one to suppose that the menstrual hemorrhage would be less abundant than normal. Be that as it may, the fact remains that in a certain number of cases, chronic endometritis is found to be associated with uterine hemorrhage. For the present it must remain a question as to whether the hemorrhage in these cases is due to the endometritis or to associated lesions, whether these be anatomic or physiologic in character. Hitschmann and Adler are strongly of the opinion that chronic endometritis, while it may cause leukorrhea, is never in itself a cause of hemorrhage. My own work inclines me strongly to the same belief. The same authors lay stress upon the essential importance of the so-called plasma cell in the microscopic diagnosis of chronic endometritis.

Hyperplasia of the Endometrium.— In 1900 and at various times since then, Cullen called attention to an interesting condition of the endometrium with which uterine bleeding is always associated clinically. To this condition the designation of hyperplasia of the endometrium was given, at

the suggestion of Dr. William H. Welch. It occurs most frequently at or near the time of the menopause, and next most frequently in young girls within the first few years of menstrual life. It may, however, be encountered at any period during the reproductive life. The characteristic clinical symptom is excessive and prolonged menstruation. Metrorrhagia is much less frequent.

Grossly the mucosa is usually much thicker than normal, and not infrequently presents a shaggy or even markedly fungous appearance. The hyperplastic change seems to affect both the epithelium and the stroma. The former is distinctly thickened, the nuclei being heavily stained and closely crowded, at times giving the impression of a number of distinct layers. The glands are uneven, some being narrow, some moderately tortuous, and some very much dilated, appearing like small cysts. (Fig. 37.) That the overdistention of the glands is not due to mere retention of their contents is indicated by the fact that the lining epithelium, instead of being flattened out, is often quite high. The smoothness of the walls and the lack of tortuosity in these large dilated glands gives them a characteristically rigid or parchment-like appearance. The stroma gives the impression of compactness and overabundance. Its hyperplastic activity is often indicated by the presence of mitoses. Although karyokinetic figures are common in the epithelium of the uterus, they are almost never observed in the normal stroma. Another finding of great frequency is the presence of numerous thromboses, as well as of large veins distended with blood, and perhaps of hemorrhagic extravasations in the tissues.

Hyperplasia of the endometrium is the common finding in cases of so-called "functional" or "idiopathic" uterine bleeding, and there is good reason to believe that it is purely secondary to an endocrine disorder, probably of the ovaries. This subject is discussed under the head of functional hemorrhage.

Muscular Insufficiency of the Uterus.— It was Scanzoni who, in 1860, first directed attention to the mesometrium as a factor in the causation of uterine hemorrhage. In his work, "Ueber die Chronische Metritis," he argued that chronic metritis frequently exists as a disease of the uterine musculature even when the mucosa is normal. According to him chronic metritis is the most common of female diseases, a view which is now obsolete. He described the disease as consisting of a primary stage of hyperemia and serous infiltration, followed by one of induration. These observations, of course, were enunciated before the days of the modern microscope. In addition to the changes in the myometrium, Scanzoni described an increase in the brittleness of the arteries, which he held to be primarily responsible for the hemorrhage.

Theilhaber, in more recent years, has also emphasized the importance of the mesometrium in both normal and pathological uterine hemorrhage. He uses the term "mesometrium" in order to embrace the connective tissue as well as the muscle, only the latter being indicated by the word "myome-

FIG. 37.— HYPERPLASIA OF THE ENDOMETRIUM.

The section is a portion of a scraping. The surface epithelium is intact, as seen at a and a. At b are two normal uterine glands. Fully half of the glands are more or less dilated. At c is an irregular and dilated gland, filled with coagulated serum. d and e are also dilated, but not spherical glands. The gland f is markedly dilated and spherical. In none of the dilated glands is there any atrophy of the epithelium. The stroma between the glands is very dense. In some of these cases large veins are scattered throughout the stroma. Given such a mucosa as this, one can say with almost absolute certainty that the patient has had very profuse menstrual bleeding (Cullen).

trium." He asserts that contraction of the uterine wall plays an important rôle in regulating the pelvic circulation, not only during pregnancy, but throughout the reproductive life of the woman. If the contractility is defective, various pathological changes occur, the leading symptom of which is a tendency to hemorrhage from the mucosa. He further states that the proportion of muscle to connective tissue varies according to the age of the individual. In childhood and in old age there is a preponderance of connective tissue over muscle, while the blood vessels are small. During the reproductive life of the woman, on the other hand, there is less connective tissue and more muscle, while the blood vessels are large. A pathological defect of muscle or an excess of connective tissue during reproductive life is the essential lesion in many conditions characterized by hemorrhagic discharge. To this general condition Theilhaber gives the name of "insufficientia uteri."

In this same group of causes may be placed that described by Anspach, who, under the name of "metrorrhagia myopathica," describes a form of uterine bleeding which he attributes to a failure of the normal increase in the elastic tissue which takes place toward the close of menstrual life, or of the normal obliterative changes in the blood vessels, or an excessive hypertrophy of connective tissue, making firm contraction of the uterus and consequent compression of the blood vessels impossible. In this way are produced disturbances of the endometrial circulation and profuse menorrhagia or metrorrhagia.

Arteriosclerosis of the Uterine Vessels.— Much importance has been attributed to this factor by Pankow, Reinecke, and a number of other authors. The blood vessel changes described by Pankow, from an examination of 55 uteri, involved the smaller arteries of the mesometrium and endometrium, and consisted in an increase in the elastic fibres of the vessels, as well as of the uterus itself. These changes were observed only in the uteri of women who had borne children. Age apparently played no part, for they were found even in very young women. These alterations differ from those commonly noted in senility in that the latter involve larger vessels by preference.

Similar studies have been made by Reinecke, Herman, Martin, Küstner, Slocum, von Kahlden, Findley, and others. The designation of "apoplexia uteri" was applied to these cases by Cruveilhier. The tendency of many gynecologists in the past seems to have been to consider that all cases of uterine bleeding for which no other explanation could be found were probably due to uterine arteriosclerosis. So far as I know, all the reported cases of uncontrollable uterine hemorrhage ascribed to arteriosclerosis were in patients who had not yet passed the menopause, and, as Barbour wisely says, "arterosclerosis after the menopause has been very frequently described, but never as accompanied by serious hemorrhage." It is obviously difficult, and sometimes impossible, to eliminate other possible causes in the consideration of these cases. No evidence has as yet been presented which

to my mind, justifies us in ascribing more than an occasional rôle to this cause.

Carcinoma of the Uterus.— In all forms of cancer of the uterus by far the most important symptom is bleeding. Especially true is this of the cervical forms, i. e., *squamous cell carcinoma* and *adenocarcinoma of the cervix*. The early stages of these growths are characterized by numberless fine filiform outgrowths from the surface of the cervix, either on the pars vaginalis, or in the cervical canal, as the case may be. These consist of a slender stem of stroma, bearing one or more thin walled vessels, and covered by a delicate epithelial surface. Their structure explains why the slightest trauma, such as that produced by coitus, or by straining efforts, may result in bleeding. At first this is slight and intermittent, but as the cancerous process continues it becomes continuous and sometimes very profuse. In the later stages the hemorrhage is due in large measure to the ulcerative process of the disease.

In *adenocarcinoma of the body* hemorrhage is somewhat less frequent than in cervical cancer, although even here it is the most important symptom. The lesser frequency of bleeding in cancer of the corpus uteri is explained by Cullen as due to the fact that the corporeal growths are less vascular than those in the cervix, and that they are well protected from external trauma. The vital importance of suspecting cancer in all cases of uterine hemorrhage at or near the age of the menopause is emphasized in Chapter XIV.

Sarcoma of the Uterus.— While far less frequent than carcinoma, sarcoma may occasionally be encountered in either the cervix or the body of the uterus. The symptoms are in a general way similar to those of carcinoma. As in the case of the latter, bleeding is the most important symptom. It does not usually appear until ulcerative processes begin, and hence may not be so early a symptom as it usually is with carcinoma.

Hydatidiform Mole.— This form of obstetrical hemorrhage is occasionally encountered by the gynecologist. It is a disease of the chorion characterized by two principal changes, viz., abnormal proliferation of the trophoblast and hydropic degeneration of the stroma. The latter change is responsible for the distention of the villi which gives rise to the characteristic grape-like appearance of the mole.

Clinically the condition manifests itself by uterine bleeding coming on usually in the first few months of pregnancy. It is therefore commonly mistaken for threatened abortion. Suspicion of hydatidiform mole is justified, if the uterus is enlarged beyond the size which is to be expected from the duration of the pregnancy. The passage of grape-like vesicles from the uterus makes the diagnosis certain. In one of my cases the diagnosis was made from one such tiny vesicle which adhered to the finger of the examining hand on withdrawal from the vagina.

Chorio-epithelioma.— Whenever bleeding persists after the removal of a hydatidiform mole, one should suspect the development of the malignant

tumor of chorionic epithelium, i. e., chorio-epithelioma. The latter may develop also after normal pregnancy or abortion. In either event the important symptom is uterine hemorrhage.

Microscopically, chorio-epithelioma is made up of cells from both layers of the trophoblast, i. e., the syncytium and the layer of Langhans. The alveolar arrangement of the cells around large blood spaces is quite characteristic. The tumor is very invasive and forms early metastases. Since the elements which make it up do not themselves differ from the cells of the normal trophoblast or of a hydatidiform mole, a diagnosis of chorio-epithelioma cannot safely be made from curettings.

FIG. 38.— RADIOGRAPH OF THE ARTERIAL SUPPLY OF THE ENTIRE UTERUS, X 1.

Nullipara aged 25; arteries injected with bismuth subcarbonate; autopsy specimen. The course of each uterine artery is shown along the side of the uterus, and from these the intrinsic uterine (arcuate) arteries arise (Sampson).

Uterine Myoma and Adenomyoma.— The most important symptom of uterine myoma is uterine hemorrhage, manifesting itself usually as menorrhagia. This is also true of adenomyoma of the uterus. Both the amount and the duration of menstruation are likely to be increased. The influence of myomata upon the menstrual function depends upon their size, and, even more, upon their location. Speaking generally, the subserous growths are much less likely to cause excessive menstruation than either the intramural or submucous tumors. The latter are especially apt to be associated with profuse bleeding.

This subject has been exhaustively studied by Sampson by means of the injection method. He divides the uterine wall into three zones: first, the peripheral (outer third), which is nourished by what he calls the "peripheral arteries;" second, the arcuate, the narrow zone in which the "arcuate vessels" lie; and, third, the radial (inner two thirds), which is nourished by the "radial arteries." (Figs. 38 and 39.) Bleeding from myomata, he explains, is due not only to congestion of the endometrial venous plexus from which the normal menstrual discharge emanates, but even more to a loss of efficiency of the uterine musculature.

He gives the following summary of the menstrual histories in the series of 150 cases of uterine myoma studied by him: "Forty-seven of the patients gave a history of not having had any disturbances in menstruation. Of these, 22 had small intramural and some small subserous myomata; 17, medium size and large intramural myomata; 5, adenomyomata and small intramural myomata; 2, large subserous and small intramural myomata; and, 1, a subserous and small intramural myoma.

"Sixty-four gave a history of profuse menstruation, often prolonged, i. e., the so-called menorrhagia, as the predominating type of abnormal bleeding.

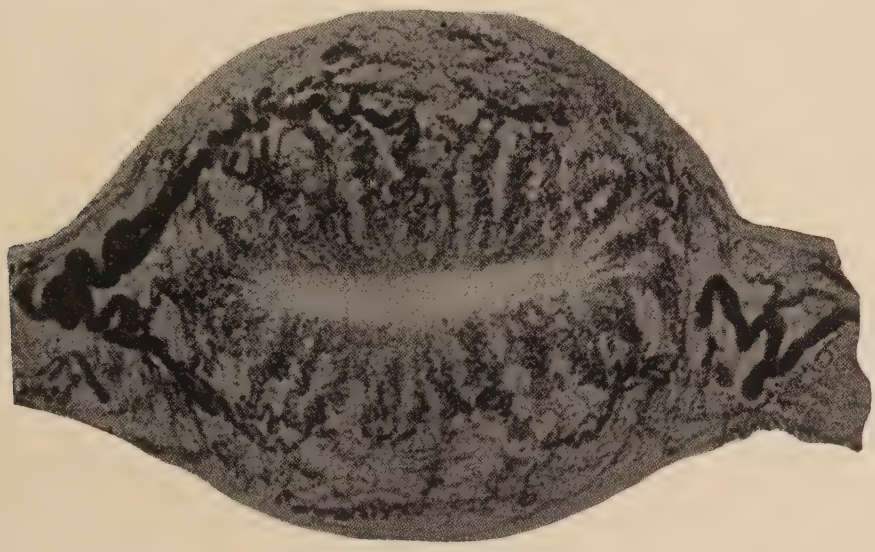

FIG. 39.— ARTERIAL SUPPLY OF THE UTERINE TISSUES, X1.

Radiograph of a cross slice 3 mm. thick of the body of the uterus. Nullipara, aged 34; arteries injected with bismuth; uterus removed for chronic pelvic peritonitis. The arcuate arteries, the large arteries, and a small portion of a third, two of which appear in the illustration, pass between the outer third and inner two thirds of the uterine wall and terminate, in the median line, in radial and peripheral branches. They divide the uterine wall into two zones — the outer or *peripheral* zone, which is nourished by peripheral branches of the arcuate arteries, and the inner or *radial* zone, which is nourished by radial branches, the latter terminating in the endometrium by fine capillaries. Each arcuate artery, with its peripheral and radial branches, supplies a quadrantal segment of the uterus, corresponding to the anterior or posterior half of the müllerian duct of that side. When the uterus is relaxed arterial blood would easily gain access to the endometrium, but when contracted it would seem that the terminal arterioles and capillaries of the radial arteries would be easily compressed (Sampson).

Thirty-nine of these had intramural tumors encroaching upon the uterine cavity as the apparent cause; in 10 a submucous tumor was present; small intramural tumors not encroaching upon the uterine cavity were found in 9; adenomyoma with other varieties of myomata were found in 5; small intramural tumors with a polyp were found in 2.

"Thirty-nine gave a history of irregular bleeding, i. e., metrorrhagia, as the predominant symptom. Carcinoma of the cervix with intramural myomata was found in 8; carcinoma of the body of the uterus with myomata in

5; polypi and small intramural tumors in 5; small intramural myomata not encroaching upon the uterine cavity, 4; large intramural myomata, 3; adenomyomata with other forms of myomata, 2; tubal pregnancy and myomata, 3; incomplete abortion with myomata and infection (one puerperal, the other probably gonorrheal), 2; hydatidiform mole with myomata. 1; sarcoma, 2. This grouping shows that any one variety may or may not alter menstruation, and that the bleeding present, especially if of the metrorrhagic type, is often due to some other condition."

Ectopic Pregnancy.— In no condition is the menstrual history of greater significance than in ectopic pregnancy. The classical picture is that of a patient who has missed one menstrual period, this being followed, after a period of from a few days to several weeks, by a slight but persistent bloody discharge. Occasionally the period of amenorrhea is longer, two menstrual periods being missed. More frequently, however, there has been no amenorrhea at all, a bloody discharge making its appearance perhaps two or three weeks after a normal menstrual period.

The characteristic hemorrhage is of the "spotting" type, the patient noticing perhaps only a few drops of blood each day. In many cases, however, bleeding is quite free. Almost always it is accompanied by some pain, more marked in one side of the pelvis than the other. Sometimes severe cramp-like attacks are observed, frequently with fainting. As in intra-uterine pregnancy, many patients experience such subjective symptoms as "morning nausea," vomiting, irritability of the bladder, etc.

Sampson has, by the injection method, studied the influence of ectopic pregnancy on the blood supply of the uterus. He finds that in these cases the uterus is enlarged, as a result of hyperemia and a thickening of the endometrium. The changes in the latter do not differ materially from those seen in early intra-uterine pregnancy.

Tuberculosis of the Generative Organs.— The most frequent seat for tuberculosis of the female genitalia is the fallopian tube. It is stated that as many as 8 per cent of all cases of salpingitis are of tuberculous origin. In the great majority of cases tuberculosis of the tube is secondary to a tuberculous focus elsewhere, although in many cases the primary focus is not ascertainable. In some cases tubal tuberculosis is only an incident to tuberculosis of the peritoneum, in which case the tubal involvement may for a considerable period be limited to the serosa. In the early stages of tubal tuberculosis, epithelial proliferation may be so marked that a branching gland-like appearance is produced. In this stage the condition might easily be mistaken for carcinoma, and such a mistake has often been made. In the later stages, the picture is more characteristically that of tuberculosis, with tubercles, giant cells, caseation, etc.

Tuberculosis of the endometrium is practically always secondary to tuberculous salpingitis. Owing to the normal cellular structure of the endometrium, tubercles of the latter do not always stand out so sharply as in most other tissues. In other cases they may be quite conspicuous.

Uterine bleeding is not an invariable accompaniment of pelvic tuberculosis, but it occurs quite frequently. As in tuberculous disease elsewhere, the associated general debility may produce amenorrhea, especially in those cases which are secondary to disease in the lungs or elsewhere. Speaking generally, excessive menstruation may be looked upon as evidencing a predominance of the local disease over the general, while amenorrhea more commonly is found in late stages, with profound deterioration of the general health.

The uterine bleeding of genital tuberculosis is practically always associated with dysmenorrhea, usually of a severe type. These two symptoms, especially when they occur together in young unmarried women, and are associated with persistent, even though slight evening fever, should lead to the suspicion of pelvic tuberculosis. Further investigation — careful family history, examination of the chest, a well kept temperature and pulse record, tuberculin tests — will often confirm this suspicion.

Inflammatory Disease of the Adnexa.— In some cases of adnexitis, menstruation may be normal in amount and rhythm; in others it is excessive in amount, with or without irregularity of rhythm. It is rarely diminished in amount. The varying effects of tubo-ovarian inflammatory disease upon menstruation are explained by Hitschmann and Adler as being dependent upon involvement or non-involvement of the ovary in the inflammatory process. While not as yet entirely proved, this view has much to support it. Certainly it is in accordance with our conception of the mechanism of the normal menstrual bleeding.

Tumors of the Ovary.— The most common tumors of the ovary are the cysts. These may be subdivided into (1) graafian follicle cysts; (2) corpus luteum cysts; (3) cystadenomata or multilocular cysts; (4) papillomatous cysts; (5) teratomata, including dermoid cysts.

The first two groups never reach a large size, and appear to exert little effect on menstruation. It has been stated that corpus luteum cysts are always associated with uterine bleeding, but a recent study of my own has shown the incorrectness of this view. Multilocular cysts, as is well known, may reach a huge size, while the remaining two groups, i. e., the papillomatous and teratomatous cysts, may also become quite large.

The effect on menstruation of any of the tumors depends on the size of the tumors, on whether they are unilateral or bilateral, and on the amount of ovarian destruction they entail. In some instances menstruation is unimpaired, in others it is excessive, while in still others it may be deficient or absent altogether. The last named phenomenon is, according to my experience, more likely to be observed with dermoids than with other ovarian cysts, perhaps because they are so frequently bilateral.

Of the solid tumors of the ovary the most important are the malignant ones, i. e., sarcoma and carcinoma. The former may be observed even in young children. Carcinoma may be primary, but is more commonly secondary, especially to pyloric cancer. This is especially so in the case of the

so-called Krukenberg tumor. Benign solid tumors are rare, fibromata being more frequent than myomata, contrary to the rule in the uterus. In none of these tumors is there any characteristic effect upon menstruation, although excessive bleeding is not uncommon.

Tumors of the Tube.— New growths in the fallopian tubes are rare, but when they occur, they are often associated with uterine bleeding. Of primary tubal neoplasms the most important is carcinoma, of which a considerable number of cases have been reported.

INTERNAL SECRETORY CAUSES OF UTERINE HEMORRHAGE

Hypersecretion of Ovary (Hyperoöphorism, Hypergonadism).— It is with the ovary that we are primarily concerned in the consideration of the internal secretory causes of menstruation. The study of the ovarian hormone, like that of the other internal secretions, is much easier along negative than along positive lines. To illustrate, by mere extirpation of the ovaries, we may show that cessation of menstruation is due to loss of the ovarian hormone. But it is far more difficult to bring about a condition of hyperfunction of the ovaries; nor is it even certain that such a condition of "hyperoöphorism," analagous to hyperthyroidism, may be produced. In the case of the thyroid, mere feeding of the gland extract to a normal person suffices to bring about hyperthyroidism. On the other hand, the possibility of producing hyperoöphorism by feeding ovarian extract is open to question. This is perhaps not surprising when we consider how little we know concerning the nature and characteristics of the ovarian hormone or hormones, and how gradual and inconspicuous would probably be the effect of an excess of ovarian secretion, even though we were sure that this could be produced by mere feeding of the extract. A number of cases have been recorded in which hyperoöphorism has apparently been brought about by the latter method. A rather striking case in the recent literature is that of Adler. It was that of a girl of 21, who had menstruated normally since the age of 15, but who after a short course of an ovarian extract for the first time in her life menstruated four days before the expected time, the flow being much more profuse and lasting longer. After the cessation of the treatment, menstruation resumed its old periodicity, duration and amount.

Much more interesting, however, is the effort of Adler to determine the existence of hyperoöphorism in an indirect manner. His method requires a word of explanation. As with the other viscera, the principal nerve supply of the uterus is derived from the sympathetic. A very revolutionary change is now in progress as regards our ideas of the physiology of the sympathetic nervous system, or, as it is frequently called, the vegetative system. According to the classical description of Langley, the entire vegetative system may be divided into two portions. First, there is the gangliated

cord which stretches along each side of the midline of the body, and which may be called the sympathetic system proper. Secondly, many of the autonomic functions of the body are in part regulated by certain cerebrospinal nerves derived principally from the brain and from the sacral portion of the spinal cord. These nerves constitute what is therefore called the craniosacral autonomic system. From the fact that the vagus nerve is the most prominent constituent, this system is also spoken of as the vagal. Kraus, again, speaks of it as the parasympathetic. The distinction between the two systems can perhaps be best illustrated by the case of the heart. This organ receives its accelerator supply from the sympathetic, its inhibitory supply from the vagus. The former is the whip of the heart, the latter the brake. This antagonism in function is characteristic, being noted in all the other organs, including the uterus.

To proceed to the practical application of these facts, it has been found that certain drugs show an elective affinity for one or the other of the two systems. Epinephrin, in accordance with the well known law of Langley, affects especially the sympathetic, its injection causing precisely the same effect on an organ as does stimulation of its sympathetic nerve supply. It is therefore spoken of as a sympathicotropic drug. On the other hand, pilocarpin is perhaps the best known of a group of drugs which exert a special action on the vagal system, and which are therefore spoken of as vagotropic drugs. To carry the point still farther, it has been found that certain endogenous chemical substances of the body, more particularly the various hormones, exhibit a special influence on one or the other of these two systems. There is reason to believe that before very long, all the various hormones of the body will be divisible into two groups, one *sympathicotropic,* the other *vagotropic.* Much has already been done along this line.

Studies on the ovarian hormone from this point of view are still very meager. The observations of Adler, however, are worthy of mention. After removal of the ovaries, and to a less extent in cases of ovarian insufficiency manifesting themselves by amenorrhea and genital hypoplasia, he found that there is an increased susceptibility to small doses of the sympathicotropic epinephrin. On the contrary, in the study of a series of cases of uterine bleeding, he observed no reaction whatsoever to epinephrin, while on the other hand there was a marked susceptibility to even very small doses of the vagotropic pilocarpin. This result he regards as justifying the view that these cases of uterine bleeding were due to overfunction of the ovary.

This conclusion, however, is open to serious question, when we consider that many structures other than the ovary contribute to the characteristic reactions. Even so, however, such work as this is of exceeding value. For perhaps the first time, we are now able to attack the hitherto rather intangible problem of the internal secretions by simple clinical methods instead of by complicated laboratory investigation. Just what practical results will accrue from this new line of endeavor remains to be seen.

Disorders of Other Endocrin Glands Than Ovary.— In addition to the ovary, practically all the other endocrin structures are also to a greater

or less extent linked up with the menstrual function, and hence may at times be responsible for uterine bleeding. This subject is discussed in Chapter XXIV.

Local Factor in Endometrium.— Another physiologic factor in the causation of uterine hemorrhage which is closely associated with the activity of the glands of internal secretion has reference to the presence of some local factor in the endometrium which is capable of diminishing the coagulability of the blood and thus predisposing to bleeding. Sturmdorf has suggested that the endometrium, under the influence of the ovarian hormone, manufactures a substance which inhibits the normal coagulability of the blood. The experimental work of Schickele and others has led to somewhat similar conclusions. Schickele's results are based on the study of the inhibiting influences of extracts and expressed juices of the uterus and ovaries on the coagulability of the blood. When there was no abnormal bleeding from the uterus, he found that the inhibitory powers of the ovarian extracts were greater than those of the uterus; but when profuse menstrual bleeding was present, it was found that the extracts from the uterus exerted a much greater inhibiting effect on coagulation. This would seem to indicate that bleeding is associated with the accumulation of coagulation inhibiting substances in the endometrium. Without going into greater detail, I need only say that the work of Schickele indicates that the inhibiting substances are formed in the ovaries and given off in the uterus. When uterine bleeding is present, there is an excessive amount of these inhibiting substances in the uterus. Schickele suggests that this is probably due to overactivity of the ovary, so that ultimately this local physiologic factor in the causation of the bleeding is apparently traceable to a fundamental disturbance in the mechanism of the menstrual process. The occasional success of the operation of curettage in the relief of uterine hemorrhage, even when the endometrium is anatomically normal, may perhaps be explained on the basis of this work, the good result being due to the removal of the inhibiting substance rather than of the endometrium.

Functional Uterine Bleeding.— There is a form of uterine hemorrhage which is often observed in the entire absence of any demonstrable pelvic disease. This type of bleeding has been spoken of variously as "functional," "idiopathic," or "essential" uterine hemorrhage. It is especially common at puberty ("hemorrhage of puberty") and at the menopause ("climacteric" or "menopausal" hemorrhage). By far the largest number of cases is observed at or about the menopausal age. The very great practical bearing of this fact is obvious, in that one is frequently called upon to distinguish between functional hemorrhage and that due to early carcinoma. This distinction is usually possible by means of, and only by means of, the microscope. Although most common at the two extremes of menstrual life, functional uterine hemorrhage may occur at any period during the reproductive life of the woman. The bleeding is characteristically of the type of menorrhagia, rather than metrorrhagia, although the latter

occasionally occurs. In some of these cases, however, the metrorrhagia is apparent rather than real, the menstrual periods being so much prolonged that bleeding is practically constant. In itself there is no pain associated with this form of uterine hemorrhage. It is interesting to note that in these cases menstruation is often delayed, and it is not infrequent to observe periods of amenorrhea, lasting, in some cases, as long as several months.

Various explanations have been offered for the mechanism of this form of menstrual disturbance. Some have explained it as due to arteriosclerosis of the uterine vessels, some as due to an " insufficientia uteri " (Theilhaber), some as due to an uterine myopathy, etc. None of these various theories, however, has seemed adequate to explain this form of hemorrhage. In a recent paper I emphasized the fact that a common histological finding in these so-called functional cases of uterine bleeding is the condition designated as hyperplasia of the endometrium (see page 235).

The Rôle of the Endocrine Glands.— The finding in these cases of such a definite structural alteration as hyperplasia would seem at first thought to speak against the functional nature of the bleeding. We must bear in mind, however, that the endometrium is, as it were, only the creature of the ovary. Certainly the remarkable cyclic changes of the uterine mucosa which are associated with normal menstruation are directly due to the internal secretory activity of the ovary. If the latter be disordered, it is natural to assume that the endometrial response will also be abnormal. In the functional hemorrhage which we are now considering, the ovarian secretion is commonly believed to be disturbed, whether primarily or secondarily. The fact that the endometrium in such cases shows the typical hyperplasia, suggests therefore that the latter may be merely the result of the disturbed endocrine function. A number of interesting facts bearing on this question may be submitted.

1. Functional uterine hemorrhage, as already stated, may occur at any age during menstrual life, but it is most common at puberty and the menopause, especially at the latter period. Exactly the same statement may be made of hyperplasia of the endometrium.

2. Hyperplasia with excessive menstruation sometimes occurs in very young individuals, in whom the possibility of an inflammatory etiology may reasonably well be ruled out. Recently I observed a typical case in a girl of twelve years, who had had profuse uterine bleeding for three months. The occurrence of hyperplasia in these very young patients, together with the frequent presence, in such cases, of other endocrinopathic stigmata, points to a probable endocrine origin. The histological picture above described as characteristic of hyperplasia of the endometrium has been described by some as of inflammatory origin. Driessen, for example, speaks of it as " endometritis necrobiotica." There does not seem to me, however, to be the slightest justification for such a belief. Certainly there is no microscopic evidence of inflammation in the typical hyperplastic endometrium.

3. It is only during the reproductive life of the woman — that is, during the period of ovarian activity — that both hyperplasia and functional bleeding are found. They disappear after the menopause and may always be checked by removal of the ovaries. Occasionally curetting, in cases of uterine bleeding occurring several months after apparent menopause, may yield a hyperplastic endometrium. These cases are analogous to the not infrequent instances of pregnancy occurring after apparent menopause. They are apparently to be explained by the fact that cessation of ovarian function is not actually complete. Or, as Schröder suggests, it is possible that the endocrine disturbance involves other endocrine glands than the ovary.

4. Hyperplasia, and the associated menstrual bleeding, are not usually cured by curettage. Observations on this point are still rather meager, owing to the fact that this endometrial condition has not as yet gained general recognition as a histological entity. The results of Schickele and Keller are, however, of interest in this connection. Of 111 curettings performed for uterine bleeding, 38 were successful and 61 were failures. Among the 38 successful cases, there were only 4 hyperplasias (10 per cent). Of the 61 unsuccessful cases, 9 were hyperplasias (15 per cent). Good results are too often taken for granted when patients with functional bleeding are curetted. Most frequently this assumption is not borne out by the subsequent history of the patient. Busse found only 10 per cent of actual cures in 506 cases of curettage for uterine hemorrhage due to various causes. He did not differentiate the cases of hyperplasia in his statistics, but there is no doubt that a great many were included, and that they would hardly show better results than the general average above quoted.

5. When a hyperplastic endometrium is curetted away it is not replaced by a normal mucosa, but by a tissue similar to that removed. This is demonstrated by the examination of sections from cases in which curettage has been repeated one or more times. The deduction to be drawn from this fact is that the lesion is not a local one, as it is, for example, in cases of the postabortive type, where curettage practically always brings about a cessation of the bleeding. In curetting cases of hyperplasia, on the other hand, we are attacking the disease at the wrong end, for we merely remove the endometrial manifestation of the underlying endocrine cause, which still remains operative.

6. In a certain number of cases curettage, especially if repeated a number of times, may result in cure. In these cases it seems likely that either spontaneously or as a result of the operative procedure there occurs a readjustment in the function of the ovary.

7. Radium and the X-ray, which destroy the graafian follicles in the ovary, exert a most beneficial effect on the type of bleeding under consideration.

8. Even if hyperplasia were a primary disease of the endometrium, it would be difficult to suggest any satisfactory explanation of the uterine

bleeding which accompanies it. By comparison, the hyperemia in cases of hyperplasia is certainly much less intense than in such conditions as acute endometritis, and yet, in the latter, menstruation is frequently normal, and may be absent altogether. In other words, disease of the endometrium without involvement of the ovary is not characteristically associated with bleeding, while disease of the ovary, even though the endometrium be normal, is frequently associated with excessive menstruation.

Is Hyperplasia a Constant Finding with Functional Uterine Hemorrhage? The question next arises as to whether all cases of functional hemorrhage are associated with hyperplasia of the endometrium. This is not an easy matter to determine, inasmuch as the exclusion of anatomic causes is sometimes impossible clinically. For instance, functional hemorrhage may be due to a concealed uterine polyp; or to a small, unrecognized myoma; or to an early carcinoma; or to a low grade adnexal involvement. Until a much larger number of cases is studied, therefore, we cannot be definite on this point. The impression that I have gained, however, from the study of a rather large number of cases, is that unless hyperplasia is found on curetting, we should not be too quick to assume the functional nature of the bleeding.

Subservience of the Endometrium to the Ovary. The conception that pathological alterations in the endometrium may be of ovarian origin is not by any means a new one. Brennecke, as far back as 1882, spoke of what he called "endometritis ovarialis." Somewhat similar ideas were suggested by Czempin, Gottschalk and Franz. These observations were published before the epoch making work of Hitschmann and Adler on the menstrual histology of the endometrium, and there is no doubt that the endometrial changes which were described really represent various stages of the premenstrual hypertrophy normally exhibited by the uterine mucosa. These earlier observations are of interest, however, in that they indicate a recognition of the habitual subservience of the endometrium to the ovary. Lauth has shown that the injection of ovarian extracts may cause hyperemia and hemorrhage, together with definite changes in the endometrium and myometrium.

The investigations of Schröder are especially interesting in this connection, in that they have to deal directly with the question of the ovarian etiology of hyperplasia. This author, from a study of 54 cases, concluded that the characteristic ovarian changes consist of a failure of follicular rupture, and a consequent absence of corpora lutea in these cases. Inasmuch as the corpus luteum is believed to be essential to the premenstrual secretory stage normally exhibited by the endometrium, it is not surprising that this secretory stage is absent in cases of hyperplasia. In other words, there is a persistence of the proliferative stage, which Schröder believes is due to the internal secretory activity of the follicles. To put it in other words, the development of the endometrium stops short of the secretory stage, the picture of hyperplasia representing merely a persistence and an exaggeration

of the proliferative phase. The conclusions of Schröder are of very great interest, but they still lack confirmation.

The Nature of the Endocrinopathy. As yet it is not possible to state whether the ovarian disorder is in the nature of excessive or of diminished function. Female hypogonadism is a frequent and well defined clinical entity, being well typified by the phenomena of the menopause, either natural or surgical. Much less is known as to the opposite condition — female hypergonadism, or hyperoöphorism. It is surprising to note the looseness with which this term has been employed by various authors. There is no scientific justification, for example, for ascribing precocious puberty to excessive secretion of the ovary, as has been done by various authors — there is, indeed, good evidence against this view. In the absence of any structural changes in the pelvic organs, it would seem logical to explain excessive menstruation as being due to excessive ovarian secretion, but this has not yet been demonstrated.

Which Ovarian Element is Concerned? It is not very satisfying, in the present state of our knowledge, to speculate as to the relative importance, in the production of hyperplasia, of the corpus luteum and the other ovarian elements. Two apparently incongruous clinical factors have struck me as bearing on this point. First, the bleeding of hyperplasia is characteristically in the nature of menorrhagia; that is, the periodicity of menstruation is usually preserved. This would suggest an influence on the part of the corpus luteum, which is preëminently the cyclical structure in the ovary. Secondly, no matter at what period the endometrium is curetted in a case of hyperplasia, the histological pattern is practically the same, although the degree of change may vary considerably, just as cases vary in the severity of their clinical symptoms. In other words, the endometrium, in cases of hyperplasia, does not exhibit the characteristic cyclic changes seen normally at the various menstrual epochs. This observation, in contrast to the one previously mentioned, would suggest that the corpus luteum influence is in abeyance. When these two observations are explained and harmonized, the problem will be well advanced toward solution. After all, little will be gained from any extended discussion of the etiology of hyperplasia until we know more concerning the nature and functions of the ovarian hormones — I use the plural number advisedly, for it seems certain that the ovary possesses more than one hormone.

The Practical Lesson to be Drawn. Too many gynecologists are inclined to explain all cases of uterine hemorrhage on the basis of some definite structural disease in the pelvis, without taking into account the importance of pathologic physiology as a possible factor. Menstruation is in itself a physiological hemorrhage, and yet no one would maintain that it is due to the hypertrophic endometrium found just before its onset. It is the ovarian secretion which is universally accepted as the ultimate cause of the phenomenon. Why then speak of an important group of cases of uterine hemorrhage as caused by hyperplasia, or even by a " local biological factor "

in the endometrium, when both the hyperplasia and the "local factor" are merely manifestations of the same underlying cause — a disordered ovarian function?

THE NERVOUS CAUSES OF UTERINE HEMORRHAGE

General Considerations.— We come, finally, to a consideration of the nervous causes of hemorrhage from the uterus. A few years ago it would have been considered only a fanciful hypothesis to attribute to the nervous system a part in the causation of uterine bleeding. When we consider, however, that such a condition as exophthalmic goiter appears often to follow severe nervous shock, and that Crile has demonstrated that the emotion of fright is associated with definite structural alterations in the brain cells, we must certainly have greater respect for the nervous system as a disturber, not only of function, but also of structure. There are many functions of the body which are essentially autonomic, but in which a vestige of voluntary control is still evident. In defecation and micturition the control of the will is still an important factor. In the case of such a function as digestion, the voluntary factor is far less important, while in the case of menstruation, to go still farther, the influence of the volitional factor is unrecognizable under normal conditions. And yet even with menstruation the higher centers still retain at least a vestigial degree of control, and under pathologic conditions, this may be greatly exaggerated.

Vasomotor Disturbance Due to Nervous or Psychic Influence.— The nervous factor in uterine bleeding has already been touched on in the discussion of the vegetative nerves as they influence the internal secretion of the ovary. It is scarcely necessary to add that what is true of their influence on the ovarian secretion is equally true as regards their influence on the other internal secretory tissues. No one can as yet say to what extent the influence of these various internal secretions on menstruation is directly chemical, and to what extent it is exerted through the medium of the vasomotor nerves. Like the vasomotor nerves in all other parts of the body, those supplying the generative organs arise ultimately from the cerebrospinal axis, the primary vasomotor center being definitely located in the floor of the fourth ventricle. The center is linked up with the psychic centers, thus explaining the occasional occurrence of uterine bleeding as a result of severe emotional disturbance of one form or another. A number of such cases have come under my own observation, of which the two following are typical:

A woman of 42, a multipara, had always menstruated regularly, the flow lasting usually about four days. A menstrual period commenced December 23, 1913. December 26, as the flow was abating, a Christmas tree in her home took fire, setting the room ablaze. The woman received a severe fright, and within a short while a profuse hemorrhage set in, lasting for six or eight hours, and then gradually abating.

A girl of 15, who had commenced to menstruate at 13, was brought to the dispensary with profuse uterine bleeding. Her menstruation had never been regular, amenorrhea being frequently noted. There had never previously been any excessive flow. The history given was that an assault on the child had been attempted on the preceding day. On account of the bleeding, it was thought that there might have been some local injury. Examination disproved this, the assault having evidently been unsuccessful. Regular menstruation, lasting three days, had occurred five weeks previously. The hemorrhage in this case was apparently due to the nervous shock associated with the attempted assault.

A number of other cases of this type might be cited. Similar cases are reported by Ehrenfest and others. That hemorrhage may be of neurotic origin has been abundantly shown by Brown-Séquard, von Recklinghausen and others. There is nothing very revolutionary in such an explanation, for many other phenomena might be mentioned which illustrate the influence of the *psyche* on processes which in themselves are essentially automatic — the "watering" of the mouth at the sight or smell of food, the acceleration of the heart from fright or joy, the sweating so characteristic of intense anxiety, etc. Even more apropos, since they illustrate the influence of psychic disturbances on the vasomotor apparatus, are such phenomena as the blush of shame or embarrassment, or the bleeding from the stomach or even from the skin which has been observed in highly nervous or hysteric women. From a theoretic point of view as well as from clinical experience, we may therefore conclude that certain cases of uterine bleeding are undoubtedly neurotic in origin, or, more properly, perhaps, "angioneurotic."

The close interlocking of the nervous system and the ductless glands make it possible for severe psychic disturbances to produce menstrual aberrations by a direct effect on the functions of the internal secretory glands. Such a phenomenon would be analogous to the glycosuria which has been shown to occur at times in conditions of severe fright and other emotional disturbance, and which is explained as being due to a nervous excitation of the adrenal bodies. This has been corroborated by the failure of the glycosuria to appear, if the nerves supplying the adrenals have previously been cut, thus severing the connection of the latter with the psychic centers. I mention this to emphasize the fact that a direct connection between the psychic centers and the ductless gland chain has been demonstrated experimentally. The nervous factor in uterine hemorrhage, like that of the internal secretions, is most apt to make itself manifest at those periods when the woman's mental equilibrium is already unstable, that is, at puberty and menopause.

TREATMENT OF UTERINE BLEEDING

Treatment of Cause.— It is almost axiomatic to emphasize that the first step in the rational treatment of uterine bleeding is the ascertainment

of the cause, and its removal if possible. The removal of polypi or of a diseased endometrium, of tumors of the uterus or adnexa, and of other causative lesions is of course the essential step in the treatment of the hemorrhage for which they are responsible. For a discussion of the operative measures which may be indicated in these cases, I would refer the reader to the various text books of operative gynecology.

Constitutional Treatment.— In all forms of uterine hemorrhage, it is of importance to correct any constitutional defect, such as anemia, diabetes, etc. When such a constitutional condition appears to be directly causative of the bleeding, its correction or treatment becomes a *sine qua non.*

Physical Measures.— In most forms of uterine hemorrhage, certain simple mechanical measures are commonly employed, and they may be of the greatest importance in controlling the bleeding.

Rest in Bed.— The first essential in all cases of severe uterine hemorrhage is to put the patient to bed. Unless this is insisted upon, other measures are apt to be of no avail. In the milder forms of menorrhagia or metrorrhagia, especially when the latter is kept up for many weeks, it is not usually possible to keep the patient in bed continuously. The greater the amount of rest in the recumbent position, however, the less the tendency to bleed, and the better the chance of spontaneous cessation.

Cold Applications to Abdomen.— The application of cold, usually in the form of the ice bag to the lower abdomen, is a measure frequently resorted to, and one which is of undoubted service. The good effect of this measure is no doubt dependent upon the contractile effect of the cold, whether direct or indirect, on the uterine musculature.

Hot Vaginal Douches.— A time honored method of treating most types of uterine bleeding, especially metrorrhagia, is by means of hot vaginal douches. To be of any value, the douche must be taken in the recumbent position. Unless instructed on this point, women sometimes attempt douching in the sitting position, as over a commode or bucket. Little good can be expected from a douche taken in this way, as the water does not reach the vaginal fornix, as it should.

To the woman who must employ douching the ordinary douche pan is of the greatest service, though not indispensable. A less convenient though serviceable method is for the woman to lie across the bed, with the hips projecting just beyond the edge and the feet resting on a chair placed close to the bed. A rubber sheet or pad, or a piece of oilcloth, protects the bed clothing and conducts the return flow to a bucket at the side of the bed. The douche can or bag is suspended several feet above the level of the patient's hips. The nozzle is introduced for a distance of about two inches and the solution then allowed to flow into the vagina. The whole process is of course greatly facilitated when the douche can be given by a nurse or attendant rather than by the patient herself, as is sometimes necessary. The fountain syringe is more satisfactory than the bulb variety, which possesses the further disadvantage of easily getting out of order.

For uterine bleeding the douche may be one of hot water alone, or of some such simple substance as normal saline, boric acid or borax solution. The temperature of the douching fluid should be as high as can well be borne by the patient. Usually this will be about 110° F., although some patients can endure a temperature of 120° F. without much discomfort. The amount should never be less than one gallon, and a larger douche is often desirable. The frequency with which the treatment should be given varies according to circumstances. In hemorrhage of moderate degree, twice a day is a good average, but when more persistent or abundant, the douche should be given at least three times each day.

Vaginal Tampons.— In cases of severe uterine hemorrhage, it is occasionally necessary to insert some form or other of vaginal tampon, usually in the form of long strips of sterilized gauze. As a rule this means of controlling hemorrhage is used only as a temporizing measure, pending more active treatment, such as curettage. This applies especially to the profuse hemorrhage sometimes seen in cases of incomplete abortion. A firm vaginal tampon, consisting perhaps of several yards of gauze packed tightly against the vaginal fornix, is often of the greatest service. Its value depends not only on the direct pressure which it exerts, but also on the fact that it excites uterine contraction, thus tending to cause cessation of the bleeding as well as expulsion of the residual gestation products. In this way instrumental or digital emptying of the uterus is often made unnecessary. A vaginal pack is also occasionally called for in the control of hemorrhage due to other causes, such as cancer or myoma of the uterus, hyperplasia of the endometrium, uterine polypi, etc.

Treatment by Drugs.— The number of drugs which have been employed in the treatment of both menorrhagia and metrorrhagia is legion. The employment of only a few, however, has been based on any principle of rational therapy, and some have little to commend them except the claims of their manufacturers.

Ergot.— Ergot has always been looked upon as the sheet anchor in the treatment of uterine hemorrhage. When its use is dictated by pharmacodynamic considerations, the results obtained are often very gratifying. The principal indication for the exhibition of ergot is bleeding of the atonic type, seen most characteristically post partum or post abortum. The direct stimulating effect of ergot upon the involuntary muscle of the uterus causes a powerful tonic contraction. No more effective means of hemostasis could be secured, and in the great majority of cases the bleeding is controlled.

The cases in which ergot rarely yields results are those in which the uterine muscle is not at fault. These embrace, of course, the largest number of cases encountered in gynecological practice. It seems unreasonable to expect much assistance from ergot where the hemorrhage is due to some definite pelvic lesion, such as uterine or ovarian tumors, adnexitis, etc. And yet it is frequently given to patients of this group.

Again, in functional hemorrhage, such as that seen at puberty or at the menopause, the use of ergot can scarcely be of much avail, for here the defect lies in the endocrine system. The point to be emphasized regarding the administration of ergot, therefore, is that its use should be confined to those cases in which there is reason for believing that atony of the uterine musculature plays an etiological rôle.

Ergot is most commonly administered in the form of the fluidextract. When a pronounced effect is desired, as for example in the prophylaxis of postpartum hemorrhage, the dose should be one dram. When its use is to be continued over a longer period, as in the treatment of moderate uterine bleeding, smaller doses are to be employed. In cases of this type I am in the habit of prescribing about twenty minims of the fluidextract every four hours. For hypodermatic administration, when called for by such emergencies as the occurrence of postpartum hemorrhage, either the official fluidextract or one of the proprietary forms of the drug may be employed hypodermically (ergotol, ernutin, etc.). The latter have come into extensive use for internal administration also.

Hydrastis.— Hydrastis, in the form of hydrastinin, is one of the most popular drugs used in the treatment of uterine hemorrhage. Its stimulating effect on the uterus is much greater than that of hydrastis, from which it is derived. Unlike ergot, it does not cause contraction of the uterine muscle, its value as a hemostatic depending upon its constricting effect upon the arterioles. Hydrastinin may be given in average doses of about one half grain of the hydrochlorid. When the fluidextract of hydrastis is employed, the dose should be about 30 minims.

Cotarnin Phthalate.— A drug which has attained considerable vogue in Europe, and to a less extent in this country, is cotarnin phthalate, or styptol. It is an oxidation derivative of the opium alkaloid narcotin. Like hydrastis, it produces a pronounced ateriolar constriction. Its advantage over the latter drug, however, lies in the fact that its action is confined to the urogenital system. It is therefore much safer than hydrastis, which may bring about a dangerous increase in blood pressure. The average dose is about three quarters of a grain every 4 hours.

Other Drugs for Internal Administration.— Other drugs which have been employed in the treatment of either menorrhagia or metrorrhagia are apiol, gossypium, cannabis indica, gallic acid, calcium salts, digitalis, etc.

Intra-Uterine Applications of Drugs.— While there are both theoretical and practical objections to the treatment of uterine hemorrhage by intra-uterine applications, this method is still warmly commended by some gynecologists. Boldt, for example, advises the use of zinc chlorid in this manner. He recommends that the application be made of longer duration by leaving within the uterus a gauze strip saturated with the medicament. From five to ten drops of a 50 per cent solution of zinc chlorid, or a somewhat larger amount of a 10 to 20 per cent solution, may be applied. A special "applicator syringe" is used to make the application. The gauze

is left in about three days. Instead of zinc chlorid, pure phenol or phenol diluted with glycerin may be used. In the latter case, the gauze should be withdrawn after a few hours.

Gerstenberg advocates the application of pure formalin to the endometrium in cases of uterine hemorrhage, especially of the climateric variety.

Injections of Blood and Serum.— Curtis calls attention to the efficacy of injections of whole blood in uterine hemorrhage. The following very simple technic is recommended: "A 20 c.cm. or larger ground glass syringe is sterilized, preferably by the drug method, and the inner surface lubricated with sterile petrolatum. Blood is withdrawn in the usual manner from a cubital vein of the donor; the needle is then inserted beneath the subcutaneous tissues of the back of the patient and the blood injected." The injections may be repeated when necessary.

Instead of whole blood, the use of human serum has been advised by Thwaite, while Kaiser advocates the use of horse serum. The last named is certainly the most convenient form of medication, for the horse serum is easily obtainable commercially. Finally, mention may be made of the injection of *coagulen* (New and Non-Official Remedies, A.M.A.), a proprietary which is said to hasten coagulation. The results in the few cases in which I have employed it have been encouraging.

Organotherapy.— See Chapter XXVI.

Treatment by Radium and X-Ray.— See Chapter XXVII.

Treatment of Functional Uterine Hemorrhage.— Among the most interesting, and also the most perplexing, problems encountered in gynecological practice is the treatment of cases of "functional," or "idiopathic," or "essential" uterine bleeding. This type, as has been stated elsewhere in this chapter, includes the numerous cases of functional climacteric hemorrhage and the less frequent instances of menorrhagia of puberty. In the majority of such cases, especially if severe, curettage is indicated, chiefly for diagnostic purposes. In the case of menopausal hemorrhage, the indication for curettage is urgent, on account of the importance of excluding carcinoma. The most common histological finding, with genuine functional bleeding, is hyperplasia of the endometrium.

Curettage in itself is rarely successful in relieving this form of uterine hemorrhage. Many gynecologists advocate a repetition of the procedure on the recurrence of the bleeding, and not infrequently patients are submitted to curettage many times. Although cures are sometimes obtained, curettage can scarcely be looked upon as a rational form of therapy in these cases, inasmuch as it merely removes a manifestation or end product of the underlying cause, which is an endocrine disorder involving the ovary.

The logical treatment of these cases would seem to be along the lines of organotherapy, but unfortunately the results of this form of treatment are still far from satisfactory. For a discussion of this subject see Chapter XXVI.

Patients with intractable functional hemorrhage are often benefited by the proper administration of radium or the X-ray (see Chapter XXVII). In the case of women at or near the menopause it is possible, and usually advisable, to bring about a complete cessation of the menstrual function. The problem is more difficult in the case of younger women in the child bearing age. Still, even here, the expert use of radium or the X-ray may result in diminution of the flow without actual cessation. The latter eventuality, however, is one of the risks of this form of treatment.

Finally, there are still many gynecologists who, in the case of severe and intractable uterine hemorrhage of this type, prefer to perform a hysterectomy. Fortunately, this is usually a simple and relatively safe procedure in cases of this group. It should, however, be looked upon as a *dernier resort,* its employment being dependent upon the consideration of such individual factors as the age of the patient, her social status, the number of children and the possible desire for further pregnancies, the duration and severity of the bleeding, etc.

XXII

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CHAPTER XXIII

VICARIOUS MENSTRUATION

Definition and Varieties.— The term vicarious menstruation is applied to certain rather rare cases in which extragenital hemorrhage, from one part of the body or another, occurs at regular intervals, corresponding to the menstrual periods. In some cases the extragenital hemorrhage appears to take the place of the normal uterine menstrual bleeding, which is altogether absent. These are the cases of the so-called *substitutional* type. In other instances menstruation occurs "per vias naturales," but some form of extragenital bleeding is noted in addition. To this type the name of *supplementary* menstrual hemorrhage is applied.

A good deal of fault has been found with the term vicarious menstruation. There is no certainty, it is stated, that the abnormal extragenital hemorrhage is really in the nature of a menstrual discharge, and hence it would seem that it might more justifiably be spoken of as a vicarious hemorrhage than as a vicarious menstruation. In the second place, as has already been stated, the hemorrhage is not always strictly vicarious, i. e., substitutional, for at times the normal menstrual flow occurs synchronously with it. In spite of these justifiable objections, however, the term vicarious menstruation has come into such general vogue that it will be difficult to displace it.

Incidence.— Vicarious menstruation must be looked upon as a relatively rare phenomenon. Indeed, a strong tendency has always been evident to doubt its existence. No less a personage than Matthews Duncan stated, as late as 1884, that he had never observed an instance of this disorder. He said, further "It is high time to give up the whole disease as a tissue of error if not of absurdity." Authentic reports of vicarious menstruation are now so numerous that there can be no question as to its occurrence. It must still, however, be regarded as a very uncommon phenomenon. There can be no doubt that a very large proportion of cases which have been reported as vicarious menstruation represent errors in diagnosis, as will be emphasized later. The statement credited to Lawson Tait is apropos in this connection, "I do not absolutely deny that there is any such thing as vicarious menstruation, but I do deny the propriety of examiners at the University of London or anywhere else asking the commonest cause of epistaxis and receiving the answer of vicarious menstruation with approval." Roth has found 225 cases recorded since 1870.

Sources of Hemorrhage.— The Nasal Mucous Membrane.— Most frequently vicarious menstruation occurs in the form of epistaxis. The

hemorrhage may be slight, but is often rather profuse, continuing intermittently throughout the normal menstrual period. In rare instances it may be alarming. No satisfactory explanation has been offered as to the frequency with which the nasal mucosa gives rise to this form of hemorrhage. The question would seem to be closely related to that of the occurrence of so-called nasal dysmenorrhea (see Chapter XX). The explanation of both these disorders appears to presuppose a histological relationship between the generative apparatus and the nose, and there is, indeed, some evidence for such a view. Cases of nasal vicarious menstruation have been reported by numerous observers (Walker, Coughlin, Macht).

The Stomach.— Next to the nasal tract, the stomach is perhaps the most frequent source of vicarious menstrual hemorrhage. In most cases the hemorrhage is slight in amount, and therefore not attended with danger to life. The long intermenstrual interval between the hemorrhages, furthermore, gives the patient an opportunity to recuperate from their effects. In the slighter grades of hemorrhage, there are often no associated symptoms whatsoever. Kuttner, for example, mentions a patient who was taken with such a hemorrhage while dining in a restaurant. Although a cupful of blood was vomited, the patient complacently finished her meal without further disturbance.

In the more severe forms the loss of blood may cause anemia, vertigo, weakness, and nausea. According to Kuttner, vicarious hemorrhages from the stomach are often preceded by bloody stools. Sometimes the hemorrhage occurs only once at the menstrual period; in other cases the vomiting of blood may be repeated many times. Darnall's patient, for example, is said to have had nine hemorrhages in one day.

Exceeding caution should be exercised in concluding that gastric hemorrhage in a given case is the result of a vicarious menstruation, on account of the much greater probability of its being due to actual stomach disease, especially ulcer. This subject will be discussed in another paragraph.

The Intestinal Canal.— While vicarious menstruation from this source is less frequently observed than that from the stomach, it occurs occasionally. Since slight or moderate intestinal hemorrhage is more easily overlooked than the vomiting of blood, it is probable that intestinal bleeding is not quite so rare as has been believed. Usually it is slight, being characterized by bloody stools during menstruation. On the other hand, one of the few fatal cases of vicarious menstruation which I have found recorded, that of Holmes, is said to have been of the intestinal type.

The Lungs.— Hemoptysis as a manifestation of vicarious hemorrhage has been described by many authors, but in a great many of the published reports it does not seem to have been conclusively established that tuberculosis was not the causative factor in the hemorrhage. On the other hand, it must be admitted that hemorrhage occurring only at the menstrual periods, whether of tuberculous origin or not, is still within the scope of application of the term vicarious menstruation. Ford's case is a good

example of this form of vicarious menstruation. His patient was a woman of 25, who had commenced to menstruate at 15. The periods were normal until the age of 19, when the patient is said to have "caught cold" during menstruation. After that there was only an occasional "show" of menstrual discharge, but at regular intervals of twenty-six days there was a pulmonary hemorrhage lasting from three to four days. Repeated lung examinations were negative. This subject is further discussed in Chapter XXV.

The Mammary Glands.— In view of the very close physiological relation between the female generative organs and the mammary glands, it is not surprising that the latter may be the seat of vicarious menstrual phenomena. Abnormal lactation at the time of menstruation has been described in a large number of cases, in virgins as well as in parous women. In the broadest sense such an occurrence may perhaps be considered a vicarious menstrual phenomenon.

More striking are the cases in which there is an actual discharge of blood from the nipple at each menstrual period. I have recently observed such an occurrence in a colored woman of 44, who was passing through the menopause. Each month there was a slight serosanguinolent discharge from both nipples, as I was able to demonstrate for myself over a period of several months. Many of the other reported cases were likewise observed at or near the menopause. Thornton's patient, on the other hand, was a virgin of 32, who found it necessary to keep a cotton tampon over each breast during the menstrual period. The bloody discharge from one of the breasts was so free that the tampon had to be changed once each day. More or less similar cases are reported by Hirschberg, Ziegenspeck, Lambinon, and others.

An unusual form of mammary participation in the menstrual process is exemplified by the case of Condit. In this the gland became swollen to twice its normal size, and "presented a very alarming picture as the skin became so generally ecchymotic as to present a complete blue black mamma." The curious feature of this case is that no discharge of any kind appeared at the nipple.

The Skin.— Bleeding from the skin, as a manifestation of vicarious menstruation, is an exceedingly rare phenomenon, although cases have been reported by Parrot, Müller, and others. In a number of these cases, such as those reported by Chambers and Anderson, the bleeding was preceded by erythema of the skin. From the area of the eruption there issued a serosanguinous fluid and later pure blood. The so-called "bloody sweat," a medical curiosity, said to have been first described by Aristotle, has been observed in a small number of apparently authentic cases. Opel quotes Collard's case of a Norwegian girl of 15, whose body, during her first menstrual period, was covered with red purpuric spots. After the administration of sudorifics, a bloody sweat appeared, the process being repeated several consecutive months. When pregnancy supervened, the sweating

ceased. As possibly throwing some light on the causation of the "bloody sweat," or "hematidrosis," it is significant that practically all the reported cases have been in markedly hysterical individuals (see Chapter XXV).

A different type of skin hemorrhage, of apparently vicarious origin, was observed in Condit's case, in which the menstrual periods were accompanied by extensive subcutaneous hemorrhages on the extensor surfaces of both legs.

The Lips.— The first case of vicarious menstruation from the mucous membrane of the lips was reported in 1909 by Hauptmann. In his case the bleeding came from the lower lip. Since Hauptmann's report, similar cases have been described by Coughlin and others.

The Eye and Eyelids.— Hemorrhage into the retina occurring with each menstrual period has been noted by Huizinga, Powell, and others. Huizinga's patient was a girl of 17, who, following an attack of dizziness and faintness, suffered with rapidly developing dimness and distortion of vision, first in the left eye, followed in a few minutes by a similar condition of the right. On examination the appearance of the fundus was that of hemorrhagic retinitis, with numerous blood spots scattered over the field. The condition cleared up after menstruation, only to return at two succeeding periods during which she was watched.

A case of vicarious menstruation from the lower eyelids has been reported by Claiborne.

Nevi.— A good example of vicarious hemorrhage from this source is furnished by the case of Condit. Fifteen days after operation for removal of the uterus and adnexa, the patient suffered the usual subjective symptoms of menstruation, while at the same time there was a hemorrhage into a nevus, the size of a split pea, which was situated over the left ninth intercostal space. As a result of the hemorrhage the little tumor became as large as a hen's egg, but in about 4 days, it diminished again by one half. This process was repeated every twenty-eight to thirty-four days for twenty-one successive months. There was never any hemorrhage from the tumor until about twenty-one months after the beginning of the vicarious swelling, at which time the tumor ruptured during a menstrual period, with the occurrence of profuse venous bleeding. The tumor was then excised, its removal being followed at the next menstrual period by the occurrence of vicarious hemorrhage in the breast gland.

The Kidneys.— Cases are recorded in which vicarious menstruation is said to have assumed the form of hematuria. Ford's patient, for example, is stated to have suffered with bleeding of this sort every month. She was thirty-two years old, very hysterical, and suffered also with a floating right kidney. The difficulties of excluding actual kidney disease in cases of this type are obvious. Cuturi and Dschigit report similar cases of vicarious menstrual hematuria.

Old Cicatrices.— Kerley reports vicarious hemorrhage from a cicatrix over the cricoid cartilage, to the left of the mid-line of the larynx, in a girl

of twenty-five. Every twenty-eight days, during the menstrual periods, this cicatrix would break and discharge from four to six ounces of blood. There was very little flow from the vagina.

Abdominal Fistulae.— A case is reported by Bircher in which there was a bloody discharge at regular monthly intervals from a fistulous tract remaining after ventrofixation of the uterus. The formation of the fistula followed the development of a large subcutaneous hematoma, and Bircher makes an interesting observation in this connection. He finds that the overwhelming majority of such postoperative hematomata occur in patients who are operated upon within a few days before menstruation begins. He suggests that the susceptibility to hematomata at this time may be due to some change in the blood, such as a lessening of its coagulability.

The Umbilicus.— A case of vicarious umbilical menstruation is reported by Gardner, whose patient was a Polish girl of sixteen. For three successive months, at the menstrual periods, there was observed a hemorrhage from the umbilicus lasting from twenty-four to forty-eight hours. Being frightened at this, she wore a tight band about the abdomen. Following this the umbilical hemorrhage is stated to have ceased, and to have been replaced by severe epistaxis and hemoptysis. It is probable that such cases of umbilical menstrual hemorrhage are due to the presence of müllerian duct remnants, as described by Cullen.

Other Seats of Vicarious Menstruation.— In addition to the above sources of vicarious menstruation, sporadic cases have been described in which the hemorrhage came from such sources as the teeth and gums (Beers), varicose and carcinomatous ulcers, the external auditory meatus, the nails, hemorrhoids, and the stumps of amputated extremities (Puech).

Menstrual History in Cases of Vicarious Menstruation.— In almost all of the reported cases of vicarious menstruation, uterine menstruation has been either absent or scantier than normal. Occasionally it is described as excessive. In a large proportion of cases menstruation is irregular, amenorrhea being frequently noted. It is especially at the extremes of menstrual life, i.e., puberty and the menopause, that the vicarious phenomenon is apt to appear. Especially frequent is it at the climacterium. A number of cases have been noted after hysterectomy, the normal flow being replaced by hemorrhage from some other organ, most frequently the nose.

Vicarious Menstruation During Pregnancy.— As a rule, vicarious menstruation ceases when pregnancy supervenes. Norton, however, reports an unusual case, in which both uterine menstruation and a severe vicarious hemorrhage from the lungs persisted throughout the entire duration of pregnancy. The patient had suffered with the vicarious hemoptysis for many years before pregnancy occurred. The uterine hemorrhage during pregnancy, as before, was slight in amount. The case was observed by Norton throughout pregnancy, which terminated in a perfectly normal confinement.

Cause of Vicarious Menstruation.— No satisfactory explanation of

this phenomenon has as yet been offered. Most of the theories which have been suggested assume that menstruation is not a local process, but that it affects the woman's entire organism. Hirschberg, for example, compares it, from this standpoint, to pregnancy, which likewise exerts a profound systemic effect on the woman. Various hypotheses have been suggested as to what this systemic effect of menstruation is. Barnes, in reviewing the explanations which have been offered for the phenomenon, mentions the following theories: (1) that it is caused by plethora; (2) that it is the result of a weakened condition of the tissues, due perhaps to heredity; (3) that it is due to an abnormality in the structure of the blood vessels; (4) that it is dependent upon a loss of the normal integument, as in the case of wounds or ulcers. More recently Condit lays emphasis upon blood pressure changes occurring at the time of menstruation. It has not, however, been satisfactorily demonstrated that menstruation is associated with important changes in blood pressure, nor would such a hypothesis explain the predilection for certain organs as the seat of the hemorrhage.

The very periodicity of vicarious menstruation suggests at once that the ovary is primarily responsible for its occurrence, just as in the case of the normal menstrual flow. The latter is apparently due to a selective action of the ovarian hormone upon the menstrual apparatus in the pelvis, especially the blood vessels and the endometrium. The substance must, however, circulate throughout the entire blood stream, as do all hormones. It is conceivable that in certain rare cases there is present in various tissues an abnormal sensitiveness to the action of the ovarian hormone, analagous to the normal receptivity to its influence of the endometrium. In the case of the nose, for example, the vestigial relationship which the latter is believed to have with the reproductive apparatus would make it easy to understand why the nasal mucosa should occasionally respond to the ovarian stimulus, with hyperemia and hemorrhage as the result.

This explanation of vicarious menstruation is not, of course, susceptible of proof in the present state of our knowledge. I mention it merely as a hypothesis, and because it impresses me as fitting in better than any other hypothesis with our newer knowledge of the phenomenon of menstruation.

Diagnosis.— The diagnosis of vicarious menstruation is never justified by observation of only one menstrual period. The *sine qua non* in the diagnosis is the regular occurrence of the abnormal extragenital hemorrhage at the menstrual epochs. It is usually necessary, therefore, to observe the patient over a period of several months, unless her history of the past periodic hemorrhages is unmistakable and reliable.

The possibilities for error in diagnosis are many and obvious. Beyond question many cases which have been reported as instances of vicarious menstruation are due to other causes, such as ulcer of the stomach, pulmonary tuberculosis, etc. The opposite error, i. e., of mistaking vicarious menstruation for such definite pathological diseases as those mentioned, is far less common. The diagnosis of vicarious menstruation should never be

made until after thorough and repeated physical examination, together with the many invaluable laboratory aids which modern medical science offers (X-ray examination, stomach analysis, urinalysis, examination of the stools, etc.).

On the other hand, the existence of a definite pathological lesion in the lungs, stomach, or elsewhere, does not preclude the occurrence of vicarious menstruation from those organs. So long as the hemorrhage takes place characteristically at each menstrual period, the diagnosis of vicarious menstruation, in the ordinary acceptation of the term, would seem to be justified.

Treatment.— Since so little is known of the cause of vicarious menstruation, its treatment must of necessity be more or less along general lines. The milder cases, especially of the nasal type, may need no treatment except perhaps rest during the menstrual periods. In the more severe cases, more vigorous measures may be necessary for the control of the bleeding. These differ somewhat according to the seat of the hemorrhage, and their consideration need scarcely be included in a work of this sort.

XXIII

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CHAPTER XXIV

MENSTRUATION AND THE ENDOCRIN GLANDS

Introductory.— The importance to the surgeon of a thorough knowledge of anatomy has long been universally recognized. It is only in recent years, however, that we have come to appreciate the value of a similar knowledge of the physiology of the various organs as related to their surgical diseases. As regards the surgery of the pelvic organs, it is perhaps true that the gynecologist has paid due respect to such conspicuous physiological phenomena as menstruation, ovulation, and pregnancy, although even these are far from being thoroughly understood. There are, however, other aspects of the physiological activities of the female reproductive organs which, while bearing with perhaps less force upon the surgery of these organs, still offer many points of interest and value, which make them well worth our careful study.

Characteristics of Endocrine Bodies.— Of especial interest is a study of the physiological connections between the pelvic organs and the various ductless glands. Viewed in a broad sense, every organ and tissue in the body possesses an internal secretory function, for each one gives off to the blood stream one or more substances capable of influencing organs and tissues far distant in the body. In the case of the so-called ductless glands (blutgefässdrüsen) the internal secretion is characterized by certain more or less striking and specific effects.

The designation of "endocrine organs" would seem to be preferable to that of "ductless glands," for the function of internal secretion is not confined to glands which possess no ducts. Perhaps the best example of a gland possessing both external and internal secretions is the testis. To the same group belongs the ovary, if we look upon the periodic discharge of ova as a species of external secretion.

The Principal Endocrine Structures, and their Importance to the Body Economy.— The principal endocrine organs, in addition to the reproductive glands, i. e., the ovary or testis, are the thyroid, parathyroid, pituitary, suprarenal, thymus, pineal body, and spleen. Our knowledge of the physiology of most of these structures is still extremely imperfect, but enough is known, in the case of some of them, to indicate how widespread and how important is their influence on the body functions. When we consider that height, weight, sexual development, and mentality, as well as many other body characteristics, are all largely dependent upon the various

internal secretions, we may well say that an individual is just about what his endocrine system makes him.

For the consideration of the entire subject of internal secretions I would refer the reader to the well known treatises of Biedl and Falta. The recent work of Bell is an excellent presentation of the relation of the internal secretions to the reproductive organs. I would also commend to the reader a perusal of the number of *Surgery, Gynecology and Obstetrics* for September of 1917, inasmuch as it is devoted to the publication of the valuable papers read in the symposium on "The Relation of the Glands of Internal Secretion to Gynecology and Obstetrics," which was held by the American Gynecological Society at its 1917 meeting.

In the present chapter it would seem proper to limit ourselves to a brief consideration of the relation of the more important endocrine glands to the reproductive organs, with special reference to their influence on the function of menstruation.

THE OVARY

The Ovary as an Endocrine Gland.— The relation of the ovary to menstruation has already been fully considered in the discussion of the causation of this phenomenon (Chapter VII). Here we need add only a word as to the general importance of the ovary in the body economy, and some of its more important connections with other endocrine glands. Although it is certain that the ovary and testis are of fundamental importance in the determination of the secondary sexual characteristics which distinguish the sexes, it must be emphasized that other endocrine glands, especially the thyroid and pituitary, play an important contributory rôle in this respect. Bell concisely sums up the evolution of our ideas concerning this subject as follows: "Van Helmont said 'Propter solum uterum mulier est quod est.' Later Chéreau changed this to 'Propter ovarium solum mulier est quod est.' Virchow in modern times reiterated this statement, and, according to Biedl, added 'All the peculiarities of her body and mind, . . . everything, in fact, which in the true woman we admire and revere as womanly, is dependent on the ovary.' But in the light of our present knowledge I venture to think that the following aphorism most accurately represents the cause and effect, 'Propter secretiones internas totas mulier est quod est.'"

The Part Played by the Ovary at Puberty and at the Menopause.— The characteristic changes brought about in the uterus and other pelvic organs at the time of puberty have already been described (Chapter IX). They are unquestionably due primarily to the inauguration of ovarian function. In the same way, the retrogressive changes of the menopause (Chapter XIII) are due to cessation of ovarian function.

Castration in Early Life.— In the human being castration is a rare operation before the age of puberty, and hence accurate observations of the results are very scanty. Experimental studies in the lower animals, however, indicate that removal of the ovaries in early life causes an inhibition of

the normal development of the sexual apparatus. Estrus, of course, fails to appear.

The Surgical Menopause and its Manifestations.— The results of castration performed during the child bearing age in women are much better known, on account of the relative frequency of double oöphorectomy during that period. In former years the operation was far more commonly done than now. Complete removal of ovarian tissue is followed by marked retrogressive changes throughout the entire generative tract, comparable to those which are normally observed at the time of the menopause. The external genitalia undergo atrophy, the skin being shriveled, and the mucosa becoming thin and anemic. Owing to the replacement of the epithelium by cicatrix-like connective tissue, there is often more or less contraction of the vagina. The uterus becomes smaller, so that the cervix is often scarcely raised above the vaginal mucosa. As at the menopause, the mammary glands undergo atrophic changes. In spite of this the breasts sometimes become much larger than before, the atrophy of the gland elements being more than compensated for by the deposit of adipose tissue. This tendency to deposit fat is in a considerable proportion of cases a general one, the woman's weight often being increased by many pounds. As an explanation for this, reference may be made to the results of Löwy and Richter, who found that castration is followed by a diminution of from 14 to 20 per cent in the oxidation processes of the body, as determined by the respiratory gaseous interchange.

As regards the effect of oöphorectomy upon the structure of other endocrine glands, Bell states that in rodents there is a " considerable increase of functional activity of the thyroid," so far as colloid production is concerned; and that there is a " certain increase in the secretory activity of the anterior lobe of the pituitary body." The thymus, he believes, undergoes hypertrophy after castration, while the effects of the operation on the suprarenal and pineal bodies are more or less uncertain.

Perhaps even more important than the anatomical changes consequent upon castration are the subjective symptoms so often observed. It is scarcely necessary to enumerate these here, for they are identical with those which are characteristic of the normal menopause, already described elsewhere (Chapter XIII). The impression has been prevalent among many gynecologists, that these symptoms are apt to be more severe the earlier in life the ovaries are removed. This, as Culbertson shows, is not borne out by the facts. I have personally been impressed with the remarkably slight subjective effect produced in many instances by removal of both ovaries, when this is necessitated in young women.

The conclusion to be drawn from our present knowledge of the subject would seem to be that the degree of menopausal reaction, whether natural or surgical, is dependent upon the individual factor, and that in all cases where conservation of healthy ovarian tissue is possible, it should be practiced. This is especially important in young individuals.

On the other hand, important as the ovary may be to a woman's well-being, it cannot be looked upon as a vital organ or even as indispensable to good health. Without both ovaries, the woman may still enjoy the best of health, and may even be spared any troublesome degree of temporary menopausal disturbance. For this reason it would seem unwise to strain conservatism to the point of saving affected ovaries in cases, for example, of extensive pelvic inflammatory disease at or near the age of the menopause, especially in the case of women who have already borne many children.

In such cases the question of subsequent pregnancy is usually of subordinate importance, the woman's sole desire being to get well and stay well. Even the most conservative of surgeons will admit that quite frequently secondary operations follow efforts at conservatism, and in the hypothetical case just mentioned it does not seem justifiable to expose the woman to this risk, in return for the slight advantage represented by the preservation for a short period of the internal secretion of the ovary. Each case must be judged on its own merits, social considerations often weighing just as heavily as cold scientific facts.

Cause of Symptoms of Artificial Menopause.— It was formerly believed that the unpleasant results produced by removal of the ovaries are dependent upon a disturbance of the nervous system. The experimental work of Knauer, and also that of Marshall and Jolly, has shown that the effects of ovarian removal are due to the withdrawal of the hormone or hormones of that organ (see Chapter VII). A modification of this view is suggested by Graves, who believes that the symptoms of the artificial menopause are the result of a "disturbance of the utero-ovarian functional harmony," rather than to mere withdrawal of the ovarian hormone.

Transplantation of the Ovaries.— A demonstration of the internal secretory function of the ovary is furnished by a certain proportion of the now large number of cases in which ovarian tissue has been transplanted in human beings. In the majority of reported cases the operation has consisted in the transplantation of ovarian tissue from the normal location to another part of the same individual (*autotransplantation*). Quite frequently, however, the procedure has been one of *homotransplantation,* i. e., from one human being to another. In a small proportion, finally, *heterotransplantation* has been attempted, ovarian tissue being transplanted from an animal of another species. Several reviews of the entire subject have lately been published, notably those of Martin, Tuffier, and Chalfant. To these the reader is referred for detailed information.

General Results.— The results so far obtained with autotransplantation have been much more successful than in the case of the other two types of operation, and it appears to have a field in a certain small proportion of cases, i. e., those in which, because of some such reason as disturbance of its blood supply, the ovary cannot be allowed to remain in its normal position. Heterotransplantation is only rarely successful, although in at least two cases it was followed by pregnancy (Croom, Morris). Even when the graft

"takes," the operation is often unsuccessful from a physiological point of view, for as a rule the transplanted ovarian tissue soon undergoes atrophy.

Operative Technic of Autotransplantation of Ovarian Tissue.—The reasons for failure in transplantation of the ovary, certainly in the case of autografts, appear to lie almost altogether in the technic employed in the operation. A number of different methods have been proposed. Tuffier, who had performed the operation of ovarian transplantation 204 times, up to July of 1914, describes his technic as follows:

"I take the ovary, or a portion of it, in a sterilized compress; the peritoneum of the abdominal wall is supported by the finger deeply inserted into the adipose tissue, and the ovary put into this opening and left there. When the glands are surrounded by adhesions they are often torn in freeing them, their surface becomes irregular, and they appear wasted. Often, also, they are sclerosed or contain cysts, but even in such instances the glands may be made use of and the results are good. If the glands are not quite aseptic, they may be dipped into tincture of iodin or passed through the flame of a lamp. The result in these cases, however, is not so good. In cases of cystic change the ovaries must be opened before grafting. A small section of the pedicle of the gland is sometimes needed to enlarge the surface for future adhesions. In some recent cases the glands were divided into equal parts and implanted separately. This is done in order to obtain the smaller grafts and larger surfaces for adhesions."

The results, in so far as the preservation of the menstrual function is concerned, have been satisfactory. This is especially true of the cases in which autografts were used. Of sixty-five of these, Tuffier states that he had interviewed thirty-seven from one to six years after operation, and found that thirty-two menstruated regularly.

The technic employed by Simpson, as detailed by Chalfant, differs somewhat from that just described. "A section measuring about 2 x 2½ cm. is cut from the cortex of the ovary to be grafted, and this is inserted, through a small skin incision, in a pocket of the subcutaneous tissue, about two inches to the inner side of the anterior superior spine of the ilium."

Present Status of Ovarian Transplantation.—The present status of the operation of ovarian transplantation is so conservatively and wisely expressed by Martin in the conclusion of his most recent paper on the subject that I can do no better than to quote him: "Careful sifting of the accumulated literature of ovarian tissue transplantation leaves a feeling of disappointment as to the surgical value in the mind of an impartial observer. Autotransplantation of ovarian tissue, as the operation is at present practiced, retards and modifies the symptoms of the artificial menopause that is precipitated by castration in a definite number of cases, depending undoubtedly upon the ability of the graft to retain its vitality in the new environment.

"The percentage of successful results in the autotransplantation seems to be as large where the simplest technic is employed, using small pieces of ovaries tucked into pockets of well vascularized tissue, as when a more com-

plicated technic is employed with an attempt to definitely couple up the blood vessels.

"The fact that homotransplants and heterotransplants are failures, made with the same technic that is employed for successful autotransplants, demonstrates that there is a definite antagonism between the tissues of different individuals of the same species, and a prohibitive antagonism between the tissues of different species.

"Occasional reports of successful homotransplants and heterotransplants encourage one to hope that in some way this antagonism of tissue will be overcome, and more successful work may result because of the greater precision this would make possible in selecting more normal tissue."

Menstruation After Removal of the Ovaries.— There are few gynecologists of experience who have not encountered cases in which menstruation has persisted, even after apparently complete removal of the ovaries. A distinction must be drawn between those in which there has been a genuine return of the function and those in which there has been merely a bloody discharge soon after the operation, without a tendency to regular recurrence. Instances of the latter type are relatively common.

"Pseudo Menstruation." — The designation of pseudomenstruation, applied to these cases by some authors, is scarcely an appropriate one, for Neu looks upon bleeding in these cases as actually menstrual in character. From the study of 54 cases in which both ovaries had been removed, he concludes that when the operation is performed after the fourteenth day of the menstrual cycle, a menstrual discharge is noted after the operation. When the latter is performed during the first fourteen days of the cycle, on the other hand, no such discharge occurs. It would seem from such observations as these that the occurrence of a postoperative menstrual discharge is explainable on the ground that, before the ovaries have been removed, a sufficient amount of their internal secretion has found its way into the blood stream to bring on the next menstrual period, even though the ovaries have meanwhile been removed. This explanation, however, is not susceptible to proof in the present state of our knowledge.

Menstruation After Apparently Complete Removal of Ovaries.— Even more interesting are the cases in which menstruation continues in a normal manner for a long period, perhaps many years, after supposedly complete removal of the ovaries. Cases of this type have been recorded by Findley, Gellhorn, and others. According to Pfister, as many as about 12 per cent of oöphorectomized women still continue to menstruate for a longer or shorter time after the operation. My own experience makes me feel that this figure is much too high. In addition to the patients exhibiting normal menstruation after such operative procedures, there are many who suffer from vicarious hemorrhages, chiefly from the nose and bowel. Finally, in about 30 per cent of castrated women, more or less well defined menstrual molimina are noted.

Theories of Persistence of Menstruation After Oöphorectomy.—

A number of theories have been advanced as to the reason for the persistence of the menstrual function after removal of the ovaries. Such clinical findings as those of Pfister, quoted above, furnished one argument to Halban in support of his contention that the ovaries themselves are not essential to menstruation, but that they exert a protective or activating influence upon some other cause, as yet unknown. This view he attempts to prove by his studies on frogs. The practical importance of Halban's distinction is not obvious. Whether the ovarian hormone is itself the sole cause of the menstrual phenomenon or whether it is an activator of some other cause seems of less importance than the observation that, in either event, the removal of the ovary practically always stops menstruation. It is now conceded by all that the menstrual function is under the influence of the entire endocrine system, but it can scarcely be denied that the ovary is the link in the ductless gland chain which is most intimately bound up with menstruation.

The explanation which is most generally accepted for this phenomenon, and the one which appeals most strongly to me, is that in all cases in which menstruation persists after oöphorectomy, a bit of ovarian tissue has been inadvertently left behind or else accessory ovarian tissue must be present somewhere in the body. There can be little question that in most cases in which menstruation continues after castration, the former condition exists, i. e., ovarian tissue has been left behind. It is difficult in many instances for even the expert operator to be sure that all ovarian tissue has been removed. Cases are recorded by Doran, Gordon and others, in which pregnancy had subsequently occurred in cases up to that time considered to exemplify a persistence of menstruation after castration. No better proof could be adduced to show that ovarian tissue must still have been present in these cases.

The question of *supernumerary ovaries* and of *accessory ovarian tissue* must also be considered in connection with this question. Certainly in the human being, the finding of accessory or aberrant ovarian tissue is rare. The studies of Meriel and others, however, indicate the possibility of this occurrence. According to Meriel such tissue may be found in various locations in the pelvis, such as the broad ligament, the ovarian ligament, etc. Cases of accessory ovarian tissue have been reported by various authors (Smith and Wood).

The possibility of this occurrence cannot be eliminated in any case of persistent menstruation after oöphorectomy, especially since the accessory ovarian bodies, according to Meriel, are ofttimes very tiny.

There seems to be no proof for the various other explanations which have been advanced for the phenomenon under discussion — the so-called "menstrual habit;" the occurrence of the "menstrual wave" in the body processes, as advanced by Jacobi and others; the possible rôle of degenerative changes in the uterine blood vessels after operation; the importance of adhesions to the uterus, etc.

THE THYROID GLAND

Evidences of Relation Between Thyroid Gland and Gonads.— In view of the fact that the thyroid, in certain of the lower types of animal life, empties its secretion directly into the uterine cavity, it is perhaps not surprising that in the human being and other higher animals, an important relation between the thyroid body and the generative system still persists, even though they be far removed anatomically. That the sexual apparatus exerts an important influence on the thyroid is suggested by a number of facts. The increased size of the thyroid often observed at puberty; the swelling of the gland during the menstrual periods, and often during pregnancy and lactation; the thyroid disturbance which may be observed at the time of the menopause; the thyroid hypertrophy seen in animals after experimental castration; the influence of sexual activity upon the thyroid, with the occasional occurrence of Graves' disease as a result of sexual excesses, and the onset, in rare cases, of even acute hyperthyroidism after oöphorectomy — all these are indicative of a close connection between the thyroid function and that of the gonads.

Thyroid Disease as a Result of Pelvic Lesions.— Cases are recorded in which thyroid disease appears clearly to have been the result of coëxisting pelvic lesions. Perhaps the most remarkable instance of this kind is the case described by Goodall and Conn. The patient, a woman of sixty-nine, complained of "pelvic trouble" of two years' duration. During the same period she had suffered also with loss of weight, tachycardia, dyspnea, and other symptoms of hyperthyroidism. The thyroid was as large as an ordinary cocoanut, while the heart was dilated, with all the signs of chronic myocarditis.

Operation was performed, after a period of preliminary treatment, on account of an ill defined pelvic mass. The condition was found to be one of advanced pelvic tuberculosis, necessitating removal of the uterus and appendages. The interesting point in the case was the fact that after the twelfth day the thyroid enlargement gradually diminished, while the symptoms disappeared. About the thirtieth day the gland was normal, and later became even smaller, so that the authors felt that she might later suffer from athyria. Six months after the operation, however, she was "remarkably well."

Menstrual Disorders Accompanying Thyroid Disease.— Further evidence of this interrelation is furnished by the menstrual disorders which are so frequently observed in connection with hyper- and hypothyroidism. In both myxedema and exophthalmic goitre menstruation is often disordered, but there is no unanimity of opinion as to the type of disturbance occurring in the two conditions. In myxedema, menstruation is most often excessive, although some authors, as for example Goodall and Conn, lay stress upon amenorrhea as a symptom of myxedema. As a matter of fact, the effect of hypothyroidism upon menstruation appears to be variable, although the evidence points to menorrhagia as more frequent than amenor-

rhea. What the factors are which determine this variability of influence it would seem unprofitable to discuss in the present imperfect state of our knowledge.

Conversely, as regards hyperthyroidism, it seems to be fairly well established that amenorrhea is more commonly associated than is menorrhagia, although here again, numerous exceptions are noted. This subject is further discussed in Chapter XXV.

THE PITUITARY BODY

General.— Although there is abundant evidence of an intimate physiological relation between the pituitary body and the generative glands, there is still much to learn of the rôle played by the various portions of the hypophysis in this connection. It is definitely established, of course, that the active principle derived from the posterior lobe (pars nervosa) exerts a powerful effect upon the involuntary muscle fibres, including the uterine musculature. It has thus come into a well deserved vogue in obstetric practice. Its other physiological effects need not be discussed in this place.

FIG. 40.— DYSTROPHIA ADIPOSOGENITALIS (Falta).

Adiposogenital Dystrophy.— Since 1901, when Fröhlich called attention to the interesting syndrome which is now well known under the designation of adiposogenital dystrophy, the influence of the pituitary in the development of the sexual glands has been recognized. The cardinal symptoms of adiposogenital dystrophy are obesity and sexual hypoplasia. In women the sexual hypoplasia manifests itself clinically through amenorrhea. Fig. 40 illustrates well the type of figure characterizing Fröhlich's syndrome.

Cases of hypopituitary amenorrhea are encountered with great frequency. I have records of a considerable number which I have observed myself. A typical history is as follows: Mrs. C., aged twenty-seven, consulted me for the purpose of finding out whether or not she

was pregnant. She had not menstruated for seven months, and had, as she expressed it, grown much larger. Forty pounds had been gained within a year. There were no subjective symptoms of pregnancy, and examination revealed that she was not pregnant. The case was evidently to be regarded as belonging to the adiposogenital group.

There has been some fluctuation of opinion as to which portion of the pituitary is concerned in these changes. The weight of evidence at the present time is, however, definitely in favor of the view that the sexual hypoplasia is a result of deficiency of the anterior lobe. It is probably true, however, that the posterior lobe is responsible for the increased carbohydrate tolerance often noted in this condition.

Influence of Pituitary on Body Growth.— It is of interest to note that the same portion of the pituitary, i. e., the anterior lobe, is looked upon as influential in the stimulation of body growth. According to Robertson, the latter is a complex process, and he believes that "an agency which causes retardation of growth at a certain stage in the development of a mammal may actually lead to acceleration of growth at some other stage in the development of the same animal." He has succeeded in isolating from the anterior lobe a potent growth controlling substance which he calls tethelin. Whether or not this substance will be of service in combating the sexual changes associated with deficiency of the anterior lobe remains to be worked out. Goetsch, on the other hand, is inclined to believe that the varying results reported by different authors as to the effect of feeding pituitary to animals are due to differences in dosage and activity of the preparation used rather than to the influence of the age of the animal. The recent experimental work of Frank, however, leads him to doubt whether the use of pituitary extracts has any stimulating effect upon the sex organs of the female.

Pituitary Hypertrophy in Pregnancy.— As in the case of the thyroid, a physiological hypertrophy of the pituitary may be observed in connection with pregnancy. This has been put beyond the realm of speculation by the work of Erdheim and Stumme, who were able to demonstrate this enlargement in pregnancy by means of X-ray studies, and who also gave an accurate description of the histological changes involved. The mild degree of hyperpituitarism associated with this form of physiological hypertrophy no doubt explains the acromegaly-like changes sometimes observed in pregnancy — the heavy, "thick" features, the enlargement of the fingers, etc. In rare cases the enlargement of the gland may be sufficient to cause symptoms suggestive of pituitary tumor, such as hemianopsia.

Pituitary Hypertrophy After Castration.— It is of significance to note that hypertrophy of the pituitary follows the operation of castration. In the case of the lower animals this has been shown experimentally by Fischera, while Tandler and Gross have demonstrated a similar change in human beings, both men and women.

THE SUPRARENAL BODIES

Difference in Function Between Cortex and Medulla.— There is a very striking difference of function between the two portions of the suprarenal body, i. e., the medulla and the cortex. The former, which developmentally is a part of the sympathetic nerve system, is also closely allied with the latter from a functional point of view. It constitutes a part of the so-called chromaffin system. The cortex, on the other hand, is developed from the mesodermic epithelium covering the fore part of the wolffian body, having the same "anlage" as the ovary or testis. It is not surprising, therefore, that the suprarenal cortex appears to exert a very important influence on the reproductive organs.

Indications of Relation Between Function of Suprarenals and Gonads.— This interesting relationship was recognized as far back as 1806, when Meckel reported a case of absence of the suprarenals and the sexual glands in an acardiac monster. He, at that time, expressed the opinion that animals possessing strong sexual powers have well developed suprarenals. It is stated that in rabbits there is a marked hypertrophy of the adrenal cortex during pregnancy, and that in birds and amphibians the adrenals increase in size during the breeding seasons. It would seem likely that similar changes occur in human beings, although no proof of this can be offered, except perhaps the observation that during pregnancy there is in some women a tendency to hirsutism, the "hypertrichosis graviditatis" of Hegar. A number of investigators (Schenk, Thumin, Soli) have found that castration in dogs and rabbits is followed by enlargement of the cortex.

Effects of Suprarenal Tumors on Reproductive System.— Our knowledge of the relations between the adrenals and the sexual system in human beings is based almost altogether upon the clinical phenomena associated with certain reported cases of suprarenal tumors. Bulloch and Sequeira, in 1905, reported a personal case of this type, and collected eleven others from the literature. Their own case, which may be considered fairly typical of the group, was that of a girl of eleven who up to the age of ten had been normal. At this age she gave evidence of precocious development. She became very stout, her face presenting the appearance of a woman of forty, whereas she had previously been pale and thin. Menstruation appeared, while her breasts became as large as those of a mature woman, and the pubes and axillae were covered with hair. At the same time a tumor developed in the abdomen.

After death the growth was found to have arisen in the left suprarenal gland, and to be composed of adrenal tissue. All the cases collected by Bulloch and Sequeira occurred in children, most of them below the age of seven. The same observation was made by Glynn, who described five additional cases in an exhaustive paper published in 1911. From a pathological standpoint, the tumors in the suprarenal are carcinomata, sarcomata, or hypernephromata.

These cases of precocious development associated with suprarenal tumors

are divided by Guthrie into two principal types, (1) the obese type, met with in both sexes; but, apart from the presence of pubic hair, the development of the sexual organs is not marked, though one of the reported female cases menstruated. (2) The muscular or "infant Hercules" type, occurring only in males, who may show true sexual precocity.

Changes in Sexual Apparatus Associated With Suprarenal Hypertrophy, Without Tumor.— It is of interest to note that sexual changes have been observed with hypertrophy of the suprarenals, in the absence of any actual neoplasm. Thirteen cases of pseudohermaphroditism. associated with "bilateral hyperplasia" of the adrenals, have been collected by Glynn. Almost all these are cases of female pseudohermaphroditism, the patients being female whose external genitalia were of the male type. In Crecchio's case the masculine resemblance was particularly striking, the patient having twice contracted gonorrhea in the rôle of a man.

Retarded Sexual Development Associated With Suprarenal Hypoplasia.— Contrasted with such observations as these upon the influence of suprarenal overgrowth upon sexual life, it is of interest to note that cases have been recorded which seem to show that retarded sexual development is sometimes associated with hypoplasia or atrophy of the adrenals. In Wiesel's case, for example, there was in a girl of eighteen an infantile condition of the genitalia. The mammae were practically absent, the nipples very rudimentary, there were no axillary hairs, and practically none on the mons veneris. Autopsy showed a striking hypoplasia of the adrenals. Similar cases have been reported by Kurakascheff, Gilford, Zander, and others.

THE PINEAL BODY

General.— This structure, which is looked upon as representing the vestigial remains of a primitive third or dorsal eye, is commonly believed to be related functionally with the sexual apparatus. The opinion most generally held is that in early life the pineal body, like the thymus, exerts an inhibitory effect on sexual development. This view is based very largely upon observations in certain cases of pineal tumor. About sixty-five or seventy authentic cases of this type have been recorded, according to McCord.

The So-Called Pineal Syndrome.— Only about 10 per cent of the entire group, however, present the clinical characters making up the "precocious macrogenitosomatic pineal syndrome." The latter, according to McCord, "is characterized by (1) overdevelopment of the sex organs, both anatomic and functional; (2) precocity of mental development; (3) general overgrowth of body with or without adiposity — the whole picture being one of early maturity." The syndrome has usually been explained as due to a hypopinealism, on the theory that pineal tumors were destructive of functioning pineal tissue. This view has been questioned by a number of investigators.

Feeding Experiments.— The most striking results in this connection, however, are those obtained by the feeding of pineal gland tissue under rigidly controlled conditions. The experiments of McCord, made on guinea pigs, showed that the symptoms usually attributed to hypopinealism "may be obtained in animals by supplying an increased amount of pineal substance by feeding or injecting pineal preparations. Such administration of pineal substances led to a more rapid growth of body than normal, and determined an early sexual maturity. The excess in rate of growth was most pronounced (40.9 per cent excess in eleven weeks) in young animals fed with pineal tissue obtained from young animals. No tendency to gigantism has followed pineal administration. After maximum size was attained, pineal administration appeared to be ineffective. Both males and females respond to the influence of pineal substances in rate of growth, but the response has been more definitely manifested in males" (McCord).

Results of Extirpation.— The results of extirpation of the pineal body by a perfected technic, as reported by Dandy, would seem to indicate that the structure is of negligible importance, none of the supposedly characteristic pineal symptoms being produced. Our knowledge of the function of this structure is confused and incomplete, and certainly no evidence exists which would indicate that it plays an indispensable, or even an important rôle, in the body economy.

THE THYMUS GLAND

Very little of a definite nature can be said with regard to the relation of the thymus to the reproductive apparatus. The fact that the gland disappears at about the time of puberty has led some to believe that it inhibits sexual development. Little scientific proof for this view has been brought forward. On the other hand, there is good reason to believe that the gland is in some way concerned with body growth. Basch's experiments showed that extirpation of the thymus is followed by loss of weight and disturbances of development of the skeleton. The recent work of Park and McClure, on the other hand, led them to conclude that, in dogs at least, the thymus body is unessential to life, and that its extirpation exerts no influence on growth or development.

More striking are the remarkable results obtained by Gudernatsch in feeding thymus and thyroid to young tadpoles. When thyroid was fed, there was a pronounced stimulation of differentiation, so that the tadpoles quickly developed into young frogs, while with thymus, on the other hand, differentiation was not accelerated, but growth was, so that instead of young frogs the thymus experiments yielded large tadpoles.

The removal of the sexual glands in animals, according to Calzolari, is followed by an increase in the size of the thymus. Paton likewise found that castration retards the normal atrophy of the thymus in guinea pigs, and that thymectomy performed before puberty is followed by an increased growth of the sexual glands.

THE MAMMARY GLAND

It has long been known that a close physiological relation exists between the uterus and the mammary gland, the most conspicuous example of this correlation of function being the phenomenon of lactation. While the primary cause of lactation has not as yet been definitely established, all the best evidence of recent years points to the generative organs as the source of the impulse giving rise to the process. The old idea that the function of the mammary gland is in some way dependent upon the nervous system would seem to have been disproved by the experiment of Ribbert, who transplanted the mammary gland of a guinea pig beneath the animal's ear, the gland developing normally and producing milk when the animal became pregnant.

In this connection the work of Starling is of interest. This observer injected virgin rabbits with extracts made from various portions of immature rabbit fetuses, and found that the mammary glands of the injected animals underwent changes similar to those seen in the glands during normal pregnancy. He concluded, therefore, that the hypertrophy of the glands seen during pregnancy is produced by a hormone formed in the body of the fetus, and that the occurrence of lactation is due to the retrograde process set up when this substance is withdrawn by the expulsion of the fetus, this retrograde process showing itself in the formation of milk. Foa has reported a large number of experiments which seem to corroborate those of Starling. Halban, on the other hand, states that the function of the mammary gland is due to an internal secretion of the ovary, except during pregnancy, when this function is temporarily assumed by the placenta, which determines the occurrence of lactation.

The most recent investigation of the subject has been made by Frank and Unger, who find fault with the results of both Starling and Halban. Their conclusions are as follows:

"1. Intra-uterine, prepuberty and puberty growth of the breasts is directly dependent on ovarian function.

"2. A cyclical change in the virgin breast occurs under the influence of the ovary.

"3. Castration does not cause rapid regression of the cyclical breast hyperplasia.

"4. No proof has been offered to show that the fetus or placenta directly produces growth of the breast in pregnancy.

"5. Evidence points to the fact that the persistent corpus luteum of pregnancy may produce this breast growth.

"6. The factors which favor or cause the persistence of the corpus luteum are unknown.

"7. Certain evidence (increase of the breast produced by hydatid mole without fetus, chorio-epithelioma) makes it unlikely that the fetus is at any time the controlling factor.

"8. Nature's process is more complicated than the simple chemical stim-

ulus assumed by Starling. As yet hyperplasia of the breasts has not been produced except by parabiosis, which does not explain the stimulus. Possibly the influence of other glands of internal secretion complicates the problem.

"9. Milk secretion is no evidence of quantitative increase in breast tissue.

"10. Under physiological conditions milk secretion sets in when the ovarian influence is removed, in the newborn after birth; in the puerpera as the corpus luteum of pregnancy regresses; sometimes postoperatively after castration in the virgin (if the breast has been activated by the corpus luteum of menstruation)."

THE PANCREAS

Not much can be said concerning the relation of the ovaries with the pancreas. Rebaudi, working in Bossi's clinic at Genoa, has reported that he has been able to demonstrate a functional connection between the ovary and the pancreas. He holds that the islands of Langerhans in the pancreas form an integral part of a great system of organs with internal secretions, and that when the function of the corpus luteum in the ovary is diminished the islands of Langerhans show a marked hypertrophy, which he regards as compensatory, the islands evidently doing an extra amount of work. According to this observer, marked changes are also seen after removal of the ovaries or the mere destruction of the corpora lutea alone. He accepts this as an evidence of the functional importance of the corpora lutea as the chief if not the only portion of the ovary concerned in the production of an internal secretion. In this indirect manner, then, he arrives at conclusions essentially similar to those reached by Fraenkel in a very different way.

XXIV

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CHAPTER XXV

RECIPROCAL RELATIONS OF MENSTRUATION AND VARIOUS DISEASES

Introduction.— Even granting that menstruation in the normal, healthy woman has practically no effect on her activities, certainly it cannot be denied that when abnormal, and especially when associated with great pain, its effect on the general health of the woman may be very great. It is not surprising, therefore, that menstruation may exert important and interesting effects upon the course of many diseases to which the woman may fall victim. Conversely, many diseases modify the regular rhythmic course of the woman's menstrual life in an equally important manner.

It is surprising how little attention has been paid to these two facts by almost all authors, including those of large systems of medicine. I have therefore thought that it might be of value to collect in one chapter what has been learned and written concerning this much neglected subject.

TUBERCULOSIS AND MENSTRUATION

General Considerations.— Owing to the extreme frequency of tuberculosis, especially of the pulmonary form, the relation of menstruation to this disease is a subject of great importance. While certain facts concerning this relationship are rather generally recognized, there are others concerning which there is as yet no unanimity of opinion. The subject may be logically discussed under two heads, as follows: (1) the influence of tuberculosis upon menstruation; and (2) the influence of menstruation upon the course of tuberculosis.

The Influence of Tuberculosis Upon Menstruation.— Amenorrhea More Common Than Menorrhagia.— When a disturbance of menstruation is associated with tuberculosis, it is most likely to be amenorrhea. Occasionally, however, menorrhagia may be observed instead, while dysmenorrhea is not by any means a rare finding. The relative frequency of amenorrhea and excessive menstruation may be gleaned from the following table by Macht, based on a study of 1600 histories from the Phipps Tuberculosis Clinic at the Johns Hopkins Hospital:

	Per cent
(1) Regular menstruation	51.6
(2) Amenorrhea	27.3
(3) Irregular menstruation	8.3
(4) Menorrhagia	4.6
(5) Pregnant or lactating	4.4
(6) In menopause, artificial or otherwise	3.8

Influence of the Age of the Patient.— Macht believes that the age of the patient is a factor of great importance in determining the regularity of the menses, and that "it is as rare to find the menstruation suppressed in patients of thirty-five years or over as it is to find it present in patients below twenty years." Of the amenorrheic patients, Macht finds that 32.5 per cent were under twenty, and 39.0 per cent between twenty and thirty, making a total of nearly three fourths below the age of thirty.

Influence of the Stage of the Disease.— Another factor of great importance — perhaps more important than the age of the patient — is the stage of the disease. Analysis of a large series of cases by Margarete Friedrich showed that, of patients suffering with the first or earliest stage of tuberculosis, 45 per cent were amenorrheic; in more advanced forms, the proportion was increased to 64 per cent, and, in even later stages of the disease, fully 85 per cent showed amenorrhea. These figures are much like those of Welch, who found amenorrhea in 11.9 per cent of early cases; in 23.7 per cent of those with two lobes diseased; and in 62.5 per cent of the most advanced cases.

Menstrual Disturbances Not Usually Dependent on Local Lesions in Pelvis.— These various statistics, and others which might be quoted to the same effect, would seem to dispose of the statement made by Veit at the Fourteenth Gynecological Congress in Münich in 1911 that, generally speaking, menstruation and ovulation are not influenced during the course of tuberculosis unless there are local pathological alterations in tubes and ovaries. The latter, he says, may be assumed to be present if a consumptive woman misses her menses and if pregnancy can be excluded. He admits, however, that amenorrhea can occasionally, though rarely, occur without local lesions in cases of advanced pulmonary tuberculosis, with marked debility.

The statements of Veit were vigorously opposed at the Congress, especially by Fraenkel and Gottschalk. They are certainly not in keeping with my own experience, nor, to judge from reports in the literature, with the experience of others. For example, the figures of Friedrich, which have been quoted above, were based on 200 cases in which the possibility of local tuberculous disease in the pelvic organs seems to have been definitely excluded. There can be little doubt, therefore, that amenorrhea is an extremely frequent concomitant of even early tuberculosis and that it is even more frequent in late stages of the disease.

While Veit is unquestionably wrong in assuming that amenorrhea in tuberculosis is always due to local involvement of the pelvic organs, the possibility of such involvement should be borne in mind in every case of pulmonary tuberculosis. In a recent paper Schiffman calls attention to the frequency with which amenorrhea, when associated with a hypoplastic uterus, is in reality found on microscopical examination to be due to tuberculous disease of the uterus or tube. In addition to two cases of his own, he mentions three reported by Ferroni, in which tuberculosis was found in

the corpus uteri of three virgins, from 12 to 14 years, who were curetted for intractable uterine hemorrhage. With tubal or uterine tuberculosis, menorrhagia is more frequent, in my experience, than amenorrhea.

Explanation of Amenorrhea in Tuberculosis.— As to the exact mechanism of amenorrhea in tuberculosis, little of a definite nature can be stated. To explain it as due to the associated anemia is merely begging the question. Hofbauer and Thaler state that tuberculous patients with amenorrhea run less favorable courses than those in whom menstruation is normal. They explain this by the fact that tubercle bacilli thrive on lipoid containing media, and that removal of the ovaries or cessation of their function brings about an excess of lipoids in the blood. In other words, the tubercle bacilli cause an inhibition of ovarian secretion and thereby a lipoidemia, which is favorable for their own growth. The work of Friedrich, however, throws serious doubt upon the views of Hofbauer and Thaler.

Practical Importance of Amenorrhea in Tuberculosis.— From a practical point of view, the amenorrhea so often observed in early phthisis is exceedingly important. I have on a number of occasions been led to suspect incipient lung lesions in girls who consulted me merely on account of amenorrhea. If cough is present, and especially if there be a rapid pulse rate and even a slight evening fever, the diagnosis of tuberculosis admits of little question. For this reason the possibility of early tuberculosis should always be borne in mind in seeking for the cause of amenorrhea, especially in young girls.

A second point worthy of remembrance is that amenorrhea in consumption may be due to the change of climate which many patients are called upon to make in the treatment of the malady.

Finally, attention may be called to the very prevalent belief among the laity that amenorrhea is a source of great danger to the girl, in that it may cause her to "go into decline," i. e., that she may develop tuberculosis. It need scarcely be said that amenorrhea in itself exerts no such effect. The belief is obviously to be attributed to the frequent association of amenorrhea and early phthisis, suggesting to the superficial observer a possible causative rôle on the part of the amenorrhea.

Menorrhagia in Tuberculosis.— Many years ago (1887) Handford called attention to the fact that menorrhagia at the beginning of menstrual life is indicative of a predisposition to tuberculosis, and that in families with a hereditary tendency to the disease, the females are apt to show early and free menstruation. While much less frequent than amenorrhea, menorrhagia is observed in a considerable proportion of cases of tuberculosis. There are some, as a matter of fact, who look upon excessive menstruation as more frequent than amenorrhea. Rosenstrauss, for example, found that among 36 patients with tuberculosis, 5 showed no change in the character of the menses, 2 a decrease in the menstrual flow, while

29 stated that with the onset of the lung affection there was an increase in the amount of the menstrual flow.

The table of Macht, given above, shows that menorrhagia was present in 4.6 per cent of his cases. This would seem to me to represent more nearly the correct proportion. Macht states that menorrhagia, when it does occur, is an early symptom of tuberculosis, preceding the amenorrhea which is more commonly observed in association with the disease. When menorrhagia occurs in the later stages of the disease, one should always bear in mind the possibility of local tuberculous disease in the pelvic organs.

Dysmenorrhea in the Tuberculous.— The paper of Eisenstein and Hollos, published in 1908, called attention forcibly to the frequency with which dysmenorrhea is associated with tuberculosis. What is more, these authors endeavored to show that the dysmenorrhea is the direct result of a general intoxication of the organism with the toxins of the tubercle bacilli. These poisonous products, they say, bring about metabolic disturbances during the years of puberty, and frequently infantilism of the genital apparatus is the result.

As a further evidence of the probable tuberculous origin of dysmenorrhea in many instances, Eisenstein and Hollos draw attention to the remarkable results of antituberculosis measures in these cases, their own plan being the administration of tuberculin. Of 70 cases of dysmenorrhea, 27 were found to be tuberculous, tubercle bacilli being found in 23, and being occult in 4. Twenty-two of these cases were treated with tuberculin and 16 were entirely cured. The result in those cases showing amenorrhea were fully as remarkable.

Gräfenburg's experience corroborates the assumption that dysmenorrhea has an underlying tuberculous basis in many cases. He found tuberculous lesions at autopsy in three young women who had been treated for dysmenorrhea. In another case of the kind, the severe abdominal pain compelled laparotomy, which revealed tuberculous lesions in the pelvic organs. He alludes to the case of Pfannenstiel, in which rapid miliary tuberculosis in the abdomen followed dilation of the cervix by means of a laminaria tent for the relief of dysmenorrhea.

Gräfenberg himself obtained positive results with the tuberculin test in 21 of 30 patients who had applied for relief from primary dysmenorrhea. The test was always negative in the cases of secondary dysmenorrhea. With the primary form, he says, the genitalia are always defectively developed. In 11 of his cases there was also a local reaction in the genitalia. These results suggest that the defective development of the genital organs is the consequence of a tuberculous process in the pelvic organs during childhood, this process subsequently undergoing healing. Dysmenorrhea in these cases is explained by the periodically recurring menstrual hyperemia. Among others who have emphasized the relation between tuberculosis and dysmenorrhea are Diepgen and Schröder.

Whether this relation is as direct as some would have us believe it is as yet difficult to say. There can be no question, however, as to the great frequency of dysmenorrhea in tuberculosis. In the later stage of the disease the menstrual pain would seem to be explainable by the greater susceptibility to pain which accompanies the lowered vitality of this stage.

In any case of dysmenorrhea in which a tuberculous etiology is suspected there is a strong indication for treatment by fresh air, sunshine, rest, good food, and, in properly selected cases, by means of tuberculin.

Influence of Menstruation Upon Tuberculosis.— General Considerations.—If the old wave theory of menstruation, as first enunciated by Goodman and later by Stephenson and Jacobi, were correct, it would be easy indeed to understand that menstruation must exert a considerable influence on the course of tuberculosis. According to this theory, it will be recalled (Chapter VIII), the menstrual periods are accompanied by a heightening of the metabolic activity and an increase in some of the body processes.

As was stated in a preceding chapter, the evidence furnished by recent investigations tends to disprove the "menstrual wave theory" (see Chapter VIII). The fact remains, nevertheless, that each menstrual period, even in the normal woman, may entail sufficient physical and psychic unrest to project it above the even tenor of her daily life. It can also be readily understood that the monthly disturbance of menstruation will be all the greater when the woman's susceptibility is increased by such a serious malady as tuberculosis.

Historical.—That the menstrual periods may influence the course of pulmonary tuberculosis has been known for many years. Indeed, mention was made of this fact by Laennec in 1879, and even earlier by Raciborski (1868). The first work in which this subject was considered in an exhaustive way was that of Daremberg, in 1880. In 1899 Neuman, in a paper before the Tuberculosis Congress, in Berlin, called attention to the fact that, at the menstrual periods, patients suffering with pulmonary tuberculosis exhibit a rise of temperature and an exacerbation of the lung symptoms. In this way, he says, the diagnosis of an otherwise latent tuberculosis may be made possible.

The same year saw the publication of the first of Turban's papers on the subject. The credit of emphasizing the importance of the menstrual influence upon the body temperature of consumptives is due, perhaps chiefly, to this author. In a second more elaborate paper, presented before the Twenty-fifth Medical Congress in Vienna in 1908, he distinguishes the several types of fever which may be exhibited by consumptive women in association with menstruation, as follows: (1) premenstrual; (2) intermenstrual; (3) postmenstrual; (4) menstrual; (5) menstrual remissions.

Premenstrual Fever in Consumptives.—Of these forms of fever the most frequent is the premenstrual, which is found in fully 73 per cent of the cases, according to Turban. Others consider its frequency much lower, Riebold giving it as only 12 per cent. It is important to bear in

mind that this premenstrual rise is purely a relative one. If it occurs in patients with very incipient tuberculosis, who have been having no fever at other times, it is shown by a slight elevation of temperature, for from a few days to a week before the onset of menstruation, to perhaps 99.5° F. or 100° F. If, on the other hand, the patient has been habitually running a slight fever, the approach of menstruation is characterized by an exacerbation.

Cornet also speaks of a premenstrual rise of temperature which he says occurs in two thirds of the cases of tuberculous disease in the female, adding that it has no influence on the course of the disease, but has a certain value in diagnosis.

Frank says that the increase of temperature is to be seen only on taking the temperature per rectum, but this is not true, since all of Turban's observations were based on temperature readings taken for ten minutes by mouth.

Kraus also found the premenstrual elevation of temperature in two thirds of his tuberculous cases. Its duration, he says, varies from ten days to two weeks, and it gives rise to no symptoms. Sometimes it is accompanied by an increase of râles, as after a tuberculin injection.

The significance of premenstrual fever, as far as the course of the disease is concerned, is usually not great. It is, however, of some prognostic importance, a very marked premenstrual elevation of fever being considered unfavorable, while slight fever at that time is usually indicative of favorable progress of the tuberculous disease.

Postmenstrual Fever.— The postmenstrual type of fever, according to Turban, is often the expression of an actual exacerbation of the lung trouble, and hence is usually a sign of bad import.

Other Types of Fever in Consumption.— The other types are much rarer in their occurrence. The intermenstrual variety of fever was described by Van Voornveldt in 1905. In the single case which he reported the rise of temperature took place, not at the menstrual periods, but regularly in the intermenstrual periods instead. This fact immediately suggests that the phenomenon may correspond with the peculiar intermenstrual pain (mittelschmerz) of which some patients complain, and which by most authors is now looked upon as due to the occurrence of ovulation at this time (Chapter XXI). This, at any rate, was Van Voornveldt's explanation of "febris intermenstrualis."

Influence of Menstruation Upon Subjective Symptoms of the Disease.— The influence of menstruation upon the subjective symptoms of tuberculosis is in some cases slight, in others quite marked. The *cough* is apt to be much more troublesome at the time of the periods. In the more advanced cases, especially, *dyspnœa* is often much exaggerated and may be quite distressing. *Râles* may become more abundant, and there may be every evidence of an actual exacerbation of the disease.

While the extra discomfort thus produced may last only through the

menstrual period, it is inconceivable that such periodic exacerbations should not exert an unfavorable influence upon the general course of the disease. Daremberg called attention to the fact that even in those cases in which amenorrhea is present a similar flareup of symptoms can still occur at intervals corresponding to the menstrual cycle.

The symptom of tuberculosis which is of greatest importance in connection with menstruation is *hemoptysis*. A considerable number of cases have been reported in which periodic hemoptysis occurs in association with the menstrual periods. Macht believes that they are not nearly so rare as they have usually been considered to be, and states that at least fifteen patients among those treated at the Phipps Tuberculosis Dispensary of the Johns Hopkins Hospital gave a history of hemoptysis occurring with the menstrual periods. Occasionally these pulmonary hemorrhages may occur in the absence of the normal menstrual flow, which they apparently replace. They then represent instances of genuine vicarious menstruation (see Chapter XXIII).

TYPHOID FEVER AND MENSTRUATION

Effect of Typhoid on Menstruation.—General Considerations.—It can not be stated that authors are agreed as to the effect exerted by typhoid fever on the menstrual process. There are some, such as Briére de Boismont and Friesinger, who assert that the effect is a powerful one and is exerted throughout the course of the disease. Others, like Peroud and Slavjanski, consider the influence of typhoid on menstruation much less noteworthy, asserting that it is noticeable only at the very beginning of the disease.

Menstruation Usually Diminished or Absent.—According to Osler and McCrae, menstruation as a rule ceases during typhoid, although it is not uncommon for it to occur at the onset of the disease. When it does so, the intermenstrual interval is apt to be shorter than normal. These authors found that menstruation was present in 11 of 483 patients during the course of typhoid fever. It was, however, never profuse, as has been reported by some.

Significance of Uterine Bleeding in the Hemorragic Type of Typhoid.—In the hemorrhagic type of the disease, uterine bleeding may occur. In patients with early and perhaps unsuspected pregnancy, it is not always easy to diagnose between the bleeding of early abortion and bleeding of menstrual character. Owing to the tendency of such febrile diseases as typhoid to cause abortion, this possibility should be borne in mind when uterine bleeding occurs during the period of onset of the disease, especially if the bleeding be at all profuse.

Variations in Effect of Typhoid on Menstruation.—Curschman states that menstruation often occurs during the early days of typhoid fever, and that it may appear before the normally expected time. In some cases, Curschman says, menstruation is normal in amount, in others it is

unusually abundant and protracted. If the onset of the fever precedes a menstrual period by two or three weeks, the flow does not as a rule appear at all. In the majority of cases, Curschman has found that amenorrhea is present throughout the course of the disease and during the first part of the convalescence. This is especially true of severe and protracted cases of typhoid, the proportion of these in which amenorrhea is noted being placed at 60 per cent. When menstruation continues during typhoid, it is usually scanty in amount. Occasionally, though rarely, rather profuse uterine hemorrhage may occur at irregular intervals, even during the febrile stage of the disease.

After severe and protracted attacks of typhoid menstruation is likely to be absent even after defervesence, perhaps for a period of two or three months. When the disease, on the other hand, has been mild, menstruation usually recurs very early in the convalescence.

Curschman lays stress upon the evil portent of profuse uterine hemorrhage occurring at the height of typhoid. This may occur in the so-called hemorrhagic type of the disease, the hemorrhage being analogous to that which is sometimes seen in the grave forms of smallpox. Barthel also, from the study of a large series of cases as far back as 1882, arrived at conclusions somewhat similar to those already discussed. He stated these as follows: (1) uterine hemorrhage, the so-called "pseudomenstruation," is not by any means common in typhoid; (2) when the menstrual period occurs within the first five days after the onset of the disease, the flow almost always appears at the regular time; (3) when the menstrual period is expected after the fourteenth day of the disease, the flow does not appear; (4) when the date of the period falls between the sixth and fourteenth days of the illness, the flow may or may not appear.

Toward the end of the disease, or during the period of convalescence, peri-uterine hematocele may occur, as was pointed out by Trousseau. Much more rare is hematometra, a case of which was reported by Martin.

Menstruation During Convalescence.— When menstruation returns after an attack of typhoid, it is as a rule either normal or subnormal in amount. Occasionally, however, the flow is very profuse, so that the patient may be considerably weakened and her convalescence retarded. Sometimes, also, women who have menstruated without pain before an attack of typhoid may complain of considerable discomfort afterward.

Effect of Menstruation Upon Typhoid Fever.—General Considerations.— Although writers on internal medicine, even the authors of the large systems, make surprisingly little mention of the influence of menstruation on the course of typhoid fever, there can be little doubt that this influence may at times be of considerable importance. This is well emphasized by Stengel, whose paper is the only exhaustive one on this subject which I have been able to find.

Importance of Relation of Menstrual Date to Time of Onset of

Disease.— Stengel states that when the onset of typhoid coincides with a menstrual period, it is apt to be very severe. This applies especially to young girls who have only recently acquired the menstrual function. The disease is perhaps most violent in its onset when the menses fail to appear, although it may be severe even when menstruation occurs. In either event, the onset of typhoid is apt to be more abrupt when it occurs at the time of menstruation, the temperature often reaching its maximum almost immediately, and remaining very high for several days. Nervous symptoms may be prominent in such cases.

Coldness, shivering, extreme sensitiveness to cold and hydrotherapeutic measures, pain in the lower part of the abdomen, and sometimes hysterical manifestations are among the symptoms which Stengel observed in these cases. Attempts to control the fever by the usual cold sponging or cold packs often increase the patient's discomfort. It can easily be understood that a diagnosis of perforation may be made on account of the sharp pain often associated with menstruation, especially when with it are observed the other symptoms above noted. I have personally seen one case in which operation was done in such a case.

Effect of Menstruation on Fever.— Not only may menstruation intensify the severity of the onset of typhoid, but it may also cause a more or less marked recurrence of the fever at the time the next menstrual period is due, whether the flow appears or not. This is shown in several cases reported by Stengel. The most striking of these was that of a lady of forty-six years, who was taken sick on May 1. After a preliminary attack of marked severity convalescence began in the early part of June, but it was interrupted in the middle of that month, as well as in July and August, by a recurrence of fever.

Each recurrence lasted about one week and was attended with remarkably severe nervous symptoms, but without any of the ordinary indications of an actual relapse. These recurrences were accurately timed to the menstrual periods, although there was no evidence of menstrual flow. After her recovery from typhoid, this patient never again menstruated, and never exhibited any of the usual symptoms of the menopause. Before the attack her menstruation had been very regular.

Influence of Menstruation on Treatment of Typhoid.— As for the management of typhoid when its onset coincides with menstruation and when the fever is high, Stengel believes that the usual cold water treatment can be only partially successful. When sponging or bathing has been used, he has observed no influence on the temperature, and, as a matter of fact, the nervous shock attending such measures may cause an actual increase of the fever. He believes, therefore, that the employment of cold in such cases should always be carefully considered, and that it must often be modified or given up altogether.

In some cases warm sponging or even bathing in water of much higher temperature than that ordinarily used is advised. Stengel considers it

bad practice to tub patients during the menstrual period. If hyperpyrexia be present, he has often obtained good results from the use of sedatives, together with the modified hydrotherapy above described. In the more severe cases, a hypodermic of morphine (about 1/6 grain) may have an immediate and lasting effect on the temperature, while in the milder cases, small doses of codein may suffice, especially if given a short time before the bath or sponge.

PNEUMONIA AND MENSTRUATION

Effect of Pneumonia on Menstruation.— According to Rosenstrauss, there is a tendency to excessive menstruation in pneumonia, especially when the onset of the disease coincides with a menstrual period. Moreover, the flow is apt to be brought on prematurely by the onset of the pneumonia. Massin, from the examination of the uterus removed at autopsy from a twenty-three year old woman who had died of pneumonia, believes that this disease, as well as typhoid and other infectious processes, causes marked pathological changes in, and perhaps total loss of, the uterine epithelium, together with a congestion of the uterine blood vessels. His findings have not been substantiated.

Occurrence of Menstruation.— The course of lobar pneumonia is usually quite short, and, when the disease falls between menstrual periods, the latter may not be materially affected, especially if the attack be mild. Griesinger (Osler and McCrae) has reported on the occurrence of menstruation during pneumonia. In one case normal menstruation occurred on the third day of an attack of pneumonia. In another case menstruation occurred on the fourth day of an attack, ten days before it was due. Beginning with the onset of the flow there were evening remissions of the temperature, followed by a slow defervescence.

OTHER INFECTIOUS DISEASES AND MENSTRUATION

Syphilis.— Syphilis appears often to be without striking effect on menstruation in the primary and secondary stages of the disease. Menorrhagia has, however, been reported as a symptom of syphilitic disease. Rosenstrauss, for example, records 13 cases of menorrhagia treated at the Charité Clinic in Berlin, in all of which the Wassermann reaction was positive and in all of whom no demonstrable pelvic lesion was found. Curettage yielded a normal endometrium in all the cases. Similar cases have been reported by others.

Meirowsky and Frankenstein have, on the other hand, called attention to the possibility that amenorrhea may be a symptom of tertiary lues. They report three cases, in which the amenorrhea had lasted from six to eight years. The patients were from twenty-eight to forty-six years of age. All were suffering with severe manifestations of tertiary syphilis

and, under the mercury and iodid given for this, menstruation was restored. In the younger women it was quite normal, but in the woman of forty-six it assumed a vicarious character, epistaxis recurring regularly at the menstrual periods. The authors emphasize the importance of specific treatment in amenorrhea in women whose history suggests the possibility of syphilis. In their opinion, the direct cause of the amenorrhea in these cases is a syphilitic involvement of the ovaries.

Influenza.— In this disease menstruation, according to Finkler, is often rather excessive. Haken has observed violent metrorrhagia in certain cases and Helling reports uterine hemorrhage during the course of influenza in a woman of forty-nine who had not menstruated for five years. The tendency of influenza to cause excessive menstruation with not infrequently an "anticipation" of the period, was a rather general observation during the recent great epidemic of the disease. This is well shown in the recent report of Esch.

Acute Exanthematous Diseases.— Observations on this subject are apparently quite rare, most of the patients with these diseases being below the age of puberty. When older individuals are affected, it would seem that the influence of such diseases on menstruation is similar to that of pneumonia and other acute infections. A rather interesting case of "menstruation during measles," in a girl of nine, has been reported by Gemmell. The day following the appearance of the characteristic eruption a discharge of blood appeared from the vagina, which Gemmell assumes to have been menstrual in character. This supposition, however, seems to me to be unjustifiable, especially since, as he says, inquiries showed that there was no renewal of the vaginal discharge after the subsidence of the measles rash.

Other Infectious Diseases.— Cholera and smallpox, according to Rosenstrauss and Massin, exert practically the same effect on menstruation as do typhoid, pneumonia and other acute infectious diseases. In leprosy, according to Morrow, menstruation is, especially in long standing cases, irregular and may cease altogether. When leprosy appears before the age of puberty, menstruation rarely appears, the disease appearing to exert an inhibitory influence on the menstrual process.

DISEASES OF THE BLOOD IN RELATION TO MENSTRUATION

Chlorosis.— Characteristics of the Disease.— As Friedrich Müller puts it, chlorosis is a "prerogative of the female sex." It has often been remarked that the frequency of this malady is on the wane in this country, and this would seem to be substantiated by the statistics of Cabot. The disease derives its name from the greenish hue of many of its victims, although it must be emphasized that this is not by any means constant. The characteristic blood changes consist in a deficiency of hemoglobin in

the red corpuscles and, to a less extent, in an actual decrease in the number of corpuscles. The plasma, according to Allbutt, is relatively increased.

Chlorosis is characteristically a disease of puberty, the usual age of the primary attack being from 14 to 21 years. It is said to be especially severe if it appears before the onset of menstruation. A first attack is rare after the age of 24. Stockman gives 23 as the highest age in a series of 63 cases. Forty-one were between the ages of 15 and 20 years.

Although the common association of amenorrhea with chlorosis has long been known, it was Virchow who first called attention to the fact that the menstrual disturbance may have an organic basis. He asserted that, together with certain other characteristic changes, a hypoplasia of the reproductive organs is an invariable finding in chlorosis. In addition he described an arrest of development in the entire arterial system, the aorta scarcely admitting the tip of the finger and the abdominal aorta being no bigger than the ordinary size of the iliac or femoral arteries.

Effect of Chlorosis on Menstruation.— In the majority of cases the symptoms of chlorosis do not appear at puberty, but some years later. Von Noorden's analysis of 215 cases showed that 56 (26 per cent) had never menstruated, while in 129 (60 per cent) there was a considerable interval between puberty and the beginning of the disease. According to Stephenson, a chlorotic diathesis tends to accelerate the age of menstrual onset. The same author finds also that before the actual onset of the chlorosis menstruation was normal in 47.5 per cent of cases; that in 20.7 per cent there was a slight deficiency; in 26.7 per cent it was markedly deficient; in 2.7 per cent it was imperfectly established; and in 2.1 per cent there was primary amenorrhea. He concludes, therefore, that "in fully one-half of the cases, the chlorotic characters, that of scantiness in amount of the discharge and increase in the interval between the periods, were stamped upon the menstrual function before the development of active chlorosis."

Amenorrhea the Common Menstrual Symptom in Chlorosis.—In by far the largest number of cases of chlorosis, menstruation is deficient or absent altogether. In a much smaller group, there may be excessive menstruation. According to Cabot, the menses were absent in 120 cases of a series of 387, they were irregular in 81, increased in 57, and unusually painful in 47. In Stockman's 63 cases, menstruation was scanty or irregular in 29, absent in 12, normal in 4, profuse in 10. In 3 menstruation had never appeared, and in 5 there was no note concerning this.

Stephenson's figures, on the other hand, show that of 177 cases there was not one with profuse menstruation either before or after the development of the disease. In one case only the discharge was described as rather free, and in 3 as too frequent, but scanty. In 2 cases menstruation remained normal. In all the remaining 171 cases, or 96.6 per cent, there was more or less marked deficiency of the menstrual flow. In 58.7 per cent it was scanty, irregular, and often painful, while in 37.8 per cent there was com-

plete amenorrhea for periods varying from two months to two years. From these various reports, therefore, it is evident that the usual effect of chlorosis is to bring about a diminution in the menstrual flow.

Menorrhagia Occasionally Observed.— When menorrhagia occurs, it may in certain cases assume very serious proportions. Doran reports a fatal case in a very anemic girl, aged 16, who had suffered with chlorosis for more than a year. The flow was scanty until shortly before death, when profuse metrorrhagia set in, resisting all treatment, including transfusion, and leading to a fatal issue. A somewhat similar case is reported by Clapham, whose patient was a girl of 18 with well marked chlorosis. The hemorrhage was so profuse that it caused syncope, vomiting, dilated pupils, and jactitation, the girl's condition becoming apparently moribund. The patient finally recovered from this attack, the subsequent periods being attended with less bleeding. Still another case of this type is recorded by Krömer.

Dysmenorrhea a Frequent Symptom.— Dysmenorrhea is a frequent symptom of chlorosis, as may be noted from the statistics of Cabot, quoted above. This is not surprising when one considers the fact that the uterus is so frequently underdeveloped in these cases, and, secondly, that the depraved vitality of the patient increases her susceptibility to pain to such an extent that a normal menstrual discomfort is magnified into actual pain.

Treatment of Menstrual Disorders of Chlorosis.— The treatment of the various menstrual disorders associated with chlorosis is fundamentally the treatment of the chlorosis itself. This has been sketched in Chapter XVIII. (See also Chapters XX and XXII.)

Effect of Menstruation on Chlorosis.— The characteristic deficiency of menstruation in chlorosis is commonly looked upon as a protective phenomenon, i. e., as an effort on the part of nature to conserve the patient's blood and strength. This idea would seem to be borne out by the observation of Sir William Gowers, who noted a fall of from 10 to 20 per cent in the number of red blood corpuscles after a menstrual period. Allbutt thinks that the cases in which there is a low count of red blood corpuscles, of perhaps 3,000,000 or less to the cubic millimetre, are those in which amenorrhea is not present, i. e., those in which menstruation is either normal or excessive.

Harmfulness of Emmenagogues.— The above facts emphasize not only the fallacy but also the actual harmfulness of the efforts which even physicians sometimes make to "bring on the flow" in cases of amenorrhea. Allbutt quotes an old medical friend as being in the habit of giving to mothers who brought their daughters for this purpose the following apt suggestion: "Madam, when the works are put in order the clock will strike."

Pernicious Anemia.— According to Rosenstrauss, the effect of pernicious anemia upon menstruation is altogether similar to that of chlorosis.

Leukemia.— Virchow long since pointed out that menstrual disorders

are very frequently associated with leukemia. Menorrhagia, sometimes associated with intermenstrual bleeding, is much more common than deficient menstruation. Virchow considers that a relation with the functions of the genital apparatus is a constant feature of leukemia. Mosler also asserts that there is a connection between uterine hemorrhage and the function of the spleen, the latter organ after such hemorrhage often showing acute enlargement, while the white corpuscles of the blood are somewhat increased in number.

Of 21 cases of leukemia, Mosler stated that in fully 16 there was some form of menstrual anomaly. In many women the menses were absent. Contrary to the findings of Virchow, Mosler found profuse menstruation in only two of his cases. In one patient the menses had not yet appeared. Noble reported a case of acute leukemia occurring in a woman of 30, in whom the malady appeared to begin with hemorrhage in the skin and mucous membranes. No pathological lesions in the generative tract were demonstrable. A somewhat similar case in a woman of 40 was reported by Hindenberg. In this case profuse bleeding took place from the nose and gums, but none from the genital tract.

Hemophilia.— In the numerous articles on this interesting disease, very little is said as to the effect on menstruation. Osler states: "In girls, menstruation is sometimes early and excessive, but happily in the female members of hemophilic families neither this function nor the act of parturition bring with them special dangers". Cases of severe menstrual bleeding in hemophilia have, however, been reported by Townsend and others.

DISEASES OF THE THYROID GLAND IN RELATION TO MENSTRUATION

Graves' Disease and Menstruation.— There is considerable discrepancy between various authors as to the effect of hyperthyroidism upon menstruation. According to some, menstruation is deficient in such cases, while others state that it is apt to be excessive. These differences of opinion are not due to faulty observation, but are almost surely to be explained by the fact that individual differences really do exist.

The two factors which suggest themselves as possibly responsible for these differences are (1) the stage of the disease under study; and (2) the type of the disease. Surgeons are familiar with the fact that the individual with Basedow's disease may exhibit marked fluctuations in the secretory activity of the thyroid gland at different times. They are also becoming more and more aware of the fact that the clinical picture of Basedow's disease may be partly due to abnormal activity of other ductless glands, in association with the thyroid. The thymus is of especial importance in this regard, as recent work has shown.

According to Allbutt, menstruation in Graves' disease is usually irregular. Amenorrhea is present in some cases, and menorrhagia in others.

Russell Reynolds, again, found menstruation to be normal in 46 of 49 cases of exophthalmic goiter.

Bloch found that menstruation was absent in 3 of a series of 12 cases of Basedow's disease which she studied. She quotes Schott as stating that the occurrence of menstruation exercises a harmful influence on the course of the disease, but believes that he is in error in this belief.

Some authors, as Kleinwächter and Hädemaker, state that in extreme cases of Graves' disease there is an atrophy of the entire genital tract, with complete amenorrhea. Others believe that the amenorrhea so often noted is due to a toxic effect exerted on the ovary.

Myxedema and Menstruation.— The same differences in the effect on menstruation which are observed with Graves' disease are noted also in myxedema. Menstruation may be absent or scanty, it may be normal, or it may be excessive. Bromwell reports a case in which it was perfectly regular in a woman of 36 who had had myxedema since the age of 25. In a case reported by Murray, on the other hand, menstruation had occurred only once in the preceding six years. After treatment with thyroid extract menstruation returned for several periods, even though the woman was over 46 years of age.

Menorrhagia is also sometimes observed and may be marked. In a case reported by Dock it seemed to be the first symptom of the disorder, being soon followed by a yellowish hue to the skin, this being at first ascribed to the loss of blood.

The relation of the thyroid to the menstrual process is further discussed in Chapter XXIV.

DIABETES AND MENSTRUATION

In many cases of diabetes, especially those of milder grades of severity, menstruation may occur quite normally. Even in the severe forms of the disease, the patient may menstruate regularly until the terminal stages of the disease. In a certain number of cases, however, amenorrhea is a symptom. Israel and Hofmeier look upon it as a frequent concomitant. Lenhartz also has found it common, and attributes it to atrophy of the generative organs. Naunyn, who has had such a tremendous experience with diabetes, states that amenorrhea occurs only in the late stages of the disease. It is therefore looked upon as due to the general debility associated with the disease.

As to the influence of menstruation upon the course of diabetes, the general impression among those who have studied this question seems to be that this is unfavorable. Naunyn is of this opinion, and believes that this fact has received too little attention from clinicians. Lecorché also holds this opinion. From a systematic study of the sugar output in a small series of cases, Rosenstrauss found that the occurrence of menstruation is often accompanied by a rise in the sugar output and occasionally by the appear-

ance of acetone in the urine. This observation is apparently borne out by a recent report of Harrop and Mosenthal.

GASTRO-INTESTINAL DISEASES AND MENSTRUATION

Effect of Menstruation on Secretory and Motor Functions of the Stomach.— In the investigation of a number of patients during menstruation, Wolfe found an increase both in the free hydrochloric acid and in the total acidity of the stomach contents. Moreover, the amount of gastric juice secreted was greater than normal. This he attributed to reflex nervous stimulation. The motor activity was found to be notably diminished. If hypersecretion be present before menstruation, it may become an actual gastrorrhea during the period. He calls attention to the fact that gastric analyses made during menstruation may give misleading results, and he urges that female patients with gastric ulcer should observe an especially strict régime at the time of menstruation, on account of the greater danger of hemorrhage at that time.

Kehrer's results are not quite so definite. He finds that the hydrochloric acid content is unchanged in normal menstruation of moderate severity, and that it is decreased in severe hemorrhage, and increased in nervous women with scanty menstruation.

Stomach Disorders and Menstruation.— Plönies observed an exacerbation of symptoms in all but 17 per cent of 450 female patients with various stomach affections. He thinks that both the sympathetic and the vagus nerve systems become hyperexcitable during this period, and that the increased vulnerability of the intestinal tract during the menstrual period imposes the necessity for strict regulation of the diet, especially to ward off relapses. Menorrhagia without other discoverable cause, he believes, is sometimes traceable to the influence of the toxins from a stomach disorder, plus the effect of the anemia and insufficient nourishment so often found with gastric disease.

Liver Diseases.— Menstrual Hyperemia of the Liver and Menstrual Jaundice (Icterus Menstrualis).— In 1872 Senator described four cases of recurring icterus appearing immediately before or during menstruation. As soon as the menstrual flow became well established, the icterus disappeared. In several of the attacks, the liver was found to be swollen, the feces decolorized, and the gastric functions disturbed. In the intermenstrual intervals the general health was unimpaired.

Senator assumed that in these cases the hyperemic condition of the liver often observed during menstruation was complicated by swelling of the mucosa of the bile passages. According to Senator, mild degrees of jaundice are often seen during menstruation. He quotes Frerichs as having described under the heading of "neuralgia of the liver" a case in which for several years there were attacks of icterus accompanied by pain and swelling of the liver immediately preceding menstruation.

Chvostek, in a study of 30 women from this standpoint, found that all but 3 of the series showed an increase in the size of the liver during the menstrual periods, the lower margin being one or two finger breadths lower than normally. There was nothing to indicate any pathologic condition in the liver, kidneys or circulatory organs. He suggests that this menstrual hyperemia of the liver may be due to the direct effect of the internal secretion of the ovary.

Cholelithiasis.— The occurrence of a menstrual hyperemia of the liver no doubt explains the exacerbations sometimes noted in hepatic and gall bladder disease at the menstrual epochs. Metzger, for example, reported a case of cholelithiasis in which icterus occurred regularly with each menstrual period. Operation revealed a gall stone which apparently could cause obstruction of the bile flow only during the hyperemia of the menstruation.

Binet, after examining 137 women with undoubted cholelithiasis, found on reviewing their histories that these patients suffered from attacks of indigestion and abdominal pain before each menstrual period. He states that, whenever in a woman gastric pains appear before the menstrual periods, biliary lithiasis should be suspected. Out of 100 women, 63 had been seen in an undoubted menstrual crisis or biliary colic. Of the 37 others, 11 had such a crisis after observation had been begun, and 26 others showed painless menstruation after they had been subjected to rigorous antilithiasis treatment.

JOINT DISEASES AND MENSTRUATION

Acute Articular Rheumatism and "Menstrual Arthritis."— It was Riebold who first called attention to what he called "acute menstrual articular rheumatism." The course of this affection, he says, is similar to that of the classic type, except perhaps for its unusual mildness in some cases. In eight of the fifteen cases which he records, only the joints of the feet were swollen and painful, and the fever was slight and transient. The heart was not perfectly normal in any of these 15 cases. A valvular defect was found in all, and was quite serious in some. The changes in the heart were thus out of all proportion to the severity of the joint lesions.

The explanation of this "menstrual arthritis," Riebold believes, is to be found in the fact that the menstruating uterus may occasionally be the source of infections. He says that fever accompanying menstruation is by no means uncommon, and is the result of the absorption of bacterial toxins or products of decomposition through the menstruating uterus. This absorptive action, he believes, is also evidenced by the occasional occurrence, with menstruation, of such affections as urticaria, erythema, herpes and neuralgia.

In a similar way, he believes that infection or intoxication from the menstruating uterus may give rise to actual polyarthritis. In one case, at least,

staphylococci were found in the blood stream, the only possible source, in Riebold's opinion, being the menstruating uterus.

A series of four cases of "menstrual arthritis" of the type described by Riebold have been reported by Morgan. One of these is of especial interest. It was that of a girl who at the age of twelve years and five months was taken with headache, fever, pain, and swelling in the joints of the knees, wrists, and shoulders successively. The case was diagnosed as rheumatism and appropriate treatment instituted, no thought being given to the menstrual function, which had not yet appeared. The next day, however, the menstrual flow appeared, the rheumatic symptoms at the same time subsiding.

What is more significant, however, is the fact that for five months these pains in the joints returned regularly at the menstrual periods, and were best governed by putting the patient to bed the day before the expected menses, and sometimes administering the salicylates. The same periodic exacerbation of symptoms at menstruation was noted also, to a greater or less degree, in the other cases reported by Morgan.

As to the influence of menstruation upon the course of an existing articular rheumatism, this, while not usually very striking, is sometimes quite evident, to say the least. This is shown in the study made by Bloch at the Basel clinic. Of a series of 76 patients with acute articular rheumatism, 53 menstruated while in the hospital; 39 of these 53 (73.58 per cent) showed no increase of symptoms at the period, while 14 (26.41 per cent) showed menstrual exacerbations. In the great majority of these cases there was a premenstrual rise of temperature, although occasionally a postmenstrual type of fever was observed.

NERVOUS AND MENTAL DISEASES AS RELATED TO MENSTRUATION

Epilepsy.— In a certain number of cases there seems to be a definite relation between epilepsy and the menstrual periods ("menstrual epilepsy"). This question has been studied by Gordon, Spratling and a number of other authors. Gordon analyzed 23 cases in which the occurrence of the epileptic attacks coincided definitely with the menstrual periods. In the intermenstrual periods all these patients enjoyed good health. The epileptic seizures always made their appearance at the onset of the menses in 5 cases, during the flow in 2 cases, at the termination of the period in 2 cases, and a day or two before menstruation in 14 cases. He states that in all these, the regularity of the attacks at the time of the periods was so striking that the patients, being able to foretell the seizures, could take the proper precautions to avoid personal injury or accident.

He cites a rather striking case, reported by Diamant, of a girl of six who had commenced to menstruate when two years old. At six the menses ceased and were replaced by epileptic seizures.

Analyzing his cases to determine the possible rôle of menstrual disorders in exciting epilepsy, Gordon finds that only 5 of his patients complained of dysmenorrhea, and that even in these gynecological treatment was followed by no amelioration in the epilepsy. He concludes, therefore, that irregularity or abnormality of menstruation has little to do with the occurrence of the epileptic seizures.

Spratling, in an earlier study of the question, arrived at conclusions essentially similar to those of Gordon. He lays stress upon the fact that menstruation, when associated with epilepsy, acts as an exciting cause merely because the predisposition to epilepsy already exists in the patient. He states his conclusions as follows:

(1) That we can, and must, in many cases of epilepsy that appear from the twelfth to the sixteenth and eighteenth year, coincident with the establishment of the menstrual flow in women, ascribe to these changes the power of inducing well defined convulsions that may be epileptic.

(2) That, except in the most remote and exceptional instances, these periods in normal individuals have no power to induce epilepsy, or even epileptoid phenomena.

(3) That, by searching carefully, we shall find in most cases of epilepsy at this period, either a previous history of convulsions, usually in infancy, or a family or personal history so tainted with a tendency to the disease that epilepsy under the stress of puberty is plainly invited.

A case reported by Maguin illustrates in a forceful way the remarkable association occasionally observed between menstruation and epilepsy. The patient was a single woman of 31 years. Her first epileptic seizure came at 17, with her first menstrual period. At 20 she became pregnant. With the cessation of menstruation came a disappearance of the epileptic attacks. On the reappearance of the menses, after the birth of the child, the attacks came on with the same regularity as before pregnancy had occurred. The seizures were typically epileptic in every way, there being no evidence whatever for suspecting a hysterical origin.

Hysteria.— The very term hysteria implies the uterine origin which was formerly ascribed to the disease. While this old supposition has of course been quite generally abandoned, it is true that menstruation frequently brings on hysterical seizures in girls or women already predisposed. This is a fact well known to every practitioner of medicine, who will recall with disgust the numerous occasions on which he has been hurriedly summoned to attend the hysterical girl in one of her monthly attacks of "unconsciousness" or "convulsions."

In many cases of this type there is associated with the hysterical attack a greater or less degree of spasmodic dysmenorrhea. The uterus is not infrequently underdeveloped and anteflexed. This is borne out by the studies of Diepgen and Schröder on 75 hysterical women. They found that menstruation in such women had as a rule commenced unusually late,

that it was often tardy, and usually scanty. This they construe as indicative of a defective development of the reproductive organs.

Insanity.— When menstruation continues in the insane woman, it may be associated with a greater or less degree of exacerbation of the mental symptoms. There is, however, a surprising lack of accurate observations on this score.

As to the influence of mental disease upon menstruation, practically all authors are agreed as to the frequency with which amenorrhea is noted among insane women. When menstruation does occur, it is apt to be scanty and irregular. Occasionally, metrorrhagia is observed in such conditions as melancholia (Allbutt and Rolleston). With improvement in the mental condition of the insane woman, there is a corresponding tendency to a restoration of the normal regularity and character of menstruation.

In a recent study of 700 feeble minded women in an institution, Swanberg and Haynes found that 425 were menstruating normally; 177 had a physiologic amenorrhea; and 108 were suffering from menstrual disturbances, chiefly irregularity, amenorrhea, and dysmenorrhea.

Since they are critical periods in the woman's life, puberty and the menopause are naturally of importance as factors in the development of mental disease, in women with a hereditary predisposition. Of the two the menopause is by far the more important, and it frequently marks the beginning of various forms of mental disorder. These, however, are discussed under a separate heading (Chapter XV).

Chronic Intoxications.— Both morphinism and alcoholism are frequently associated with a condition of amenorrhea. In lead poisoning, on the other hand, Oliver states that menstruation is apt to be increased, in many cases occurring every two or three weeks. In a few cases, however, amenorrhea is noted.

THE MENSTRUAL DERMATOSES

Occurrence of the Menstrual Dermatoses.— In a certain number of cases a definite association may be observed between menstruation and various skin eruptions, or other dermatoses. Among the authors who first called attention to the occurrence of these menstrual dermatoses were Stiller, in 1877, and Schramm, in 1878. Both of these writers looked upon the skin eruption as brought about in some reflex manner by the menstrual phenomenon. Pauli (1880) and others observed such eruptions in amenorrhea, and considered them to be a species of vicarious menstrual manifestation.

In the light of our modern knowledge of the rôle of the internal secretions in the causation of menstruation, it is probable that the menstrual skin eruptions are in some unknown manner brought about by the action of these internal secretions, either of the ovary or of the other internal secretory glands. It would be of no value to speculate as to the mechanism involved.

That the function of the reproductive organs may be linked up in some way with the activity of the skin is illustrated by the well known pigmentation so characteristic of pregnancy, as well as by the growth of hair about the genitals and in the axillae at the time of puberty. It is not surprising, therefore, that occasionally one encounters various skin conditions in association with the menstrual function. It may be of interest to discuss briefly the more important menstrual dermatoses which have been described.

Herpes.— The most frequent skin disorder noted at the menstrual periods is herpes. The most common seats of the herpetic eruption are the external genitalia, the face, the thighs, and the buttocks. As far back as 1853, Legendre had observed the frequency with which genital herpes is associated with the menses. Of 877 cases of genital herpes studied by Bergh, 644 or 73.4 per cent were of menstrual origin. There are women in whom almost every menstrual period is accompanied by herpes. On the other hand, herpes vulvaris is practically unknown among girls who have not begun to menstruate.

The lesions of herpes genitalis are usually found on the labia majora, and occasionally, according to Opel, on the cervix or on the vaginal wall. Sometimes genital and facial herpes are observed synchronously. In rare cases, especially in prostitutes, genital herpes may be so extensive as to cause marked swelling of the genitalia, with perhaps suppuration and ulceration.

Janowsky and Schwing report an unusual instance of menstrual herpes in which the eruption involved the dorsal surfaces of both hands. An even more remarkable case was that of Landesberg, who observed a herpetic eruption on the cornea in six consecutive menstrual periods in a girl of 15. The herpes in this case was accompanied by violent ciliary neuralgia.

Urticaria.— The occurrence of urticaria with menstruation was first described by Hebra. Interesting cases of this type have been reported by Schramm, Joseph, Schatz, and Pick. Opel speaks of a case of menstrual urticaria in which the eruption ceased to appear after the correction of the existing pelvic lesions (anteflexion and endocervicitis). I have encountered several cases of troublesome urticaria in women at the age of the menopause.

Angioneurotic Edema.— This interesting vasomotor disturbance is not very common, but when it occurs it is apt to be associated in some way with the menstrual phenomenon. Osler mentions six cases in which such an association was noted, the attacks in these patients being most likely to occur at the menstrual periods. He states also that at the menopause vasomotor phenomena of this type are not infrequent, patients often complaining, not only of numbness, but also of localized and transitory swellings of the hands, feet, or face.

Erythema.— This may appear either in a diffuse or circumscribed form. Frequently there may be scarcely visible erythematous splotches on the cheeks, forehead, thigh or other parts of the body. According to Opel,

they are sometimes observed only in association with the first menstruation, while in other cases more or less extensive erythema may be noted at each period.

A case of *erythema multiforme* occurring with each menstrual period was reported by the late Dr. George M. Edebohls, the patient being a girl of nineteen. The eruption was always seated upon the right side of the face, and always ran the same course, the erythema increasing in intensity until the third day of the flow, when vesicles formed over the surface. These dried into thin crusts on the fourth day, the latter falling off a few days later. The entire process repeated itself at the next menstruation.

A more severe form of erythema, which may even simulate eczema or erysipelas, has been described by certain French authors under the name of erysipéle cataménial (Greletty) or pseudo-erysipelas (Godot). Cases of this type have also been reported by Wagner and Joseph.

Erysipelas.— It is difficult, in view of the specific etiology of genuine erysipelas, to conceive of its regular occurrence with each menstrual period. Cases of this type have, however, been recorded by no less an authority than Virchow, who speaks of menstrual erysipelas occurring regularly in a girl of 18 who had acquired the disease originally during a menstrual period. Opel suggests that such cases may be due to an increase at the menstrual periods of the virulence of bacteria which may be retained in the skin of such patients.

Acne.— It is a well known fact that acne is frequently observed in girls at or near the age of puberty, and that the skin condition frequently seems to become worse at the time of the menstrual periods. Behrend reported a case in which each menstruation was preceded by the appearance of a single acne pustule on the nose, upper lip or chin. At other times there was no sign of an eruption anywhere on the body. Stiller speaks of a case in which acne pustules, accompanied by much itching, appeared on the dorsal surfaces of both hands and feet before each menstrual period, in a woman of 45. The eruption promptly disappeared when menstruation ceased. Gerber described a case of acne rosacea of the nose, occurring with each menstrual period.

Ecchymoses.— Menstrual ecchymoses were first described by Stiller. In his case they occurred a few days before each menstruation for a year and a half, the eruption consisting of irregular bluish spots on the chin, upper lip, or other parts of the face. After the period, these spots became yellowish and disappeared. Wilhelm observed a case in which for a year similar ecchymoses were noted on the thighs and sometimes also on the legs, in an otherwise normal woman of 29. In addition to these cases of subcutaneous ecchymosis, actual bleeding from the skin has been described in connection with menstruation. (See Chapter XXIII.)

Erythema Nodosum.— Cases of erythema nodosum associated with menstruation have been reported by Hobbs and by Opel. The latter's patient was a woman of 33, who for half a year had suffered with painful

nodes on the anterior surfaces of each leg, and also on the extensor surfaces of the left arm. The nodes always appeared a few days before menstruation and usually disappeared about 8 days after the onset of the flow. While the eruption was present, the patient suffered with some fever, headache, lassitude, insomnia, and constipation, together with local pain and tenderness.

Skin Pigmentation.— The discoloration of the eyelids and the dark rings under the eyes so frequently observed in menstruating women are well known. Exaggerated instances of this discoloration, in which the eyelids assume a blackish blue color, have been described by Leroy de Méricourt under the name of "chromokrinie." He explains the discoloration as due to the exhalation of pigments from the blood. This is, of course, purely a hypothesis.

Pigmentation may also be noted in other parts of the body, as illustrated by the case described by Barié. His patient was a woman of neurotic temperament, 24 years old. For 5 months menstruation was preceded by the appearance on both surfaces of the hand of peculiar dark yellowish spots. The two hands were alternately affected each month. The affected hand perspired freely, with tingling, numbness, etc. With the disappearance of menstruation, the spots also disappeared. If they were rubbed with a moist linen cloth, they assumed a light brownish color. If the cloth were saturated with oil, the spots became rusty in hue. With dilute sulphuric acid the spots became almost black.

XXV

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CHAPTER XXVI

THE ORGANOTHERAPY OF MENSTRUAL DISORDERS

Introductory.— Although Claude Bernard is commonly credited with the discovery of the internal secretions, it was Brown-Séquard, some thirty-four years later, who first directed attention to the therapeutic possibilities of organ extracts. On a memorable evening, June 1st, 1889, he announced the remarkable rejuvenating effects produced in himself by the subcutaneous injection of testicular extract. The unwarranted hopes produced by this enthusiastic report have long since been dissipated. Furthermore, the miraculous results which were claimed for this early experiment in organotherapy are perhaps chiefly responsible for the unreasonable attitude of many clinicians toward the whole subject of organotherapy. There are many whose use of these substances is based, either consciously or unconsciously, upon the notion that their therapeutic effects are, or should be, more or less specific. Unless they are — unless, for example, the success in a given case is at least comparable to the brilliant results of thyroid treatment in myxedema — there is a tendency to be discouraged and to look upon the whole treatment as unsatisfactory.

As a matter of fact, organotherapy should be looked upon as only a species of drug treatment. Like the drugs which we use in combating disease, the organ extracts are definite chemical substances. In the case of at least one of them, adrenalin, we know the exact chemical composition. Only a relatively small proportion of drugs in common use — quinin, mercury and salvarsan are the best examples — are specifics against certain diseases. The great majority are useful because they are effective against certain individual manifestations of disease. In the same way, the organ extracts, with the single exception of thyroid extract, are often employed to exert an adjuvant rather than a specific effect. Viewed in this light, and considering the relative newness and lack of development of this form of medication, there would seem to be no justification for discouragement with the results so far achieved.

Organ Extracts Which May Be Used in the Treatment of Menstrual Disorders

General Considerations.— The female generative apparatus is more or less closely linked up with a number of endocrine glands. (Chapter XXIV.) Most important, of course, is the ovary. Other ductless glands

which influence the reproductive activities are the thyroid, the pituitary, the suprarenals, the thymus and the pineal body. It is not surprising that extracts prepared from all these organs have been employed in the treatment of disorders of menstruation. Esch has recently explained the paradoxical results so often observed with organotherapy on the basis that the action of the organ extracts is often general rather than specific, due to the presence in them of protein bodies. In the case of extracts from the suprarenal, thymus, and pineal bodies, the results are as yet so vague and uncertain that it would seem unprofitable to discuss them here. I believe it will be accepted that in the organotherapy of menstrual disorders, the physician's armamentarium may, for practical purposes, be limited to extracts made from the *thyroid, ovary* and the *pituitary* body.

Unfortunately, the various commercial preparations of these substances vary so much in potency that it would seem unwise, in the present discussion, to be too dogmatic in suggesting a definite dosage of these extracts. The lack of standardization is particularly conspicuous in the case of the many forms of ovarian or corpus luteum extracts which have been put upon the market. For obvious reasons, it would be in poor taste to discuss by name the preparations of various reliable pharmaceutical firms, especially since an abundance of literature on each product is usually easily obtainable. Only the general principles governing this method of treatment need be here considered.

Thyroid Extract.— In many ways the most satisfactory of all the organic extracts in the treatment of menstrual disorders is thyroid extract. Hertoghe's statement that "the best method of stimulating the ovary, testicle, suprarenal, and hypophysis is by way of the thyroid, which governs and controls all the internal secretory organs," is perhaps not capable of scientific proof, but it has much to commend it from a practical point of view. While theoretically the influence of thyroid should be less direct and less potent in menstrual disorders than that of ovarian substance, these considerations are more than counterbalanced by the greater reliability of thyroid preparations, by our more precise knowledge of their pharmacodynamics, and by the greater potency of their action in general. A great advantage in thyroid medication is the fact that administration of the extract by mouth, most commonly in the form of the well known tablets, yields eminently satisfactory results.

Pituitary Extract.— The now well known pituitary extract, prepared commercially under a variety of names (pituitrin, hypophysin, infundibulin, etc.), is derived from the posterior lobe of the hypophysis. Its value in an increasing number of conditions is well recognized. Most brilliant, perhaps, have been its results in such obstetrical conditions as uterine inertia, postpartum hemorrhage, etc. Its value as a diuretic and as an enterokinetic, and perhaps even more, its remarkable virtue in the control of diabetes insipidus, are also worthy of note. As yet it can hardly be said to have earned a place of much importance in the treatment of menstrual

disorders, even though its employment in certain of the latter is based upon very rational indications. Encouraging results have, however, been reported by a number of investigators, and it is possible that a wider experience may demonstrate that it has a definite place in the treatment of certain disorders of the menstrual function.

It is prepared in both a solid form, for administration by mouth, and in the form of the solution, suitable for hypodermic administration. So far the results of the ingestion method have been distinctly disappointing. Whether this is due to defective methods of preparation or to a nullifying effect of the gastro-intestinal secretions cannot be stated. By far the most effective method of giving pituitary extract, however, is by the hypodermic method, for which purpose the substance is commercially prepared in ampoules suitable for hypodermic injection. Most commonly the injections are made subcutaneously, but by some the intravenous method is highly recommended.

In addition to the posterior lobe extracts, preparations of the anterior lobe alone, as well as of the entire pituitary, are available commercially. They are prepared in either powdered or tablet form.

Extract of Ovary or Corpum Luteum.— Since the ovary is the organ which directly controls the menstrual function, it would seem that quantitative disorders of the latter would most logically be treated by administration of the active principle of the ovary. While in certain menstrual disorders ovarian extract has yielded results which are very encouraging, in other types, as will be shown, the results have been more or less disappointing. The probabilities are that at least two, and perhaps more, hormones are produced in the ovary. It seems to have been fairly well established that the hormone which is responsible for the occurrence of menstruation is formed by the corpus luteum (Chapter VII). The internal secretion which is concerned with the fixation of the ovum in the first portion of pregnancy, on the other hand, more probably is derived from the so-called interstitial glands, i. e., the thecalutein cells of atretic follicles, or from the paralutein cells of the corpus luteum, which I described in a recent paper. As to this point, however, there is as yet no definite proof.

Finally, we must not overlook the fact that, according to the best evidence, the ovaries in females, like the testes in males, determine the development of the so-called secondary sexual characteristics, such as the height and configuration of the body, the distribution of hair, the character of the voice, the development of the breasts, etc. What portion of the ovary is concerned with this function is not known. From the fact that corpora lutea ordinarily are not present until menstruation is inaugurated, it seems possible that the stroma of the ovary may be the important element in this respect. At any rate, it would seem justifiable to conclude that the constituent of the ovary most directly concerned with the function of menstruation is the corpus luteum, and that other ovarian elements are probably

more important in the regulation of such phenomena as growth, determination of the secondary characteristics, etc.

I mention these matters because they appear to throw some light on the much discussed question of whether we should employ extracts made from the corpus luteum alone or from the entire substance of the ovary. Based on the above considerations, I have personally been inclined to the use of corpus luteum preparations in the management of disturbances revolving about the menstrual function. On the other hand, in cases which involve endocrinal relationships more profoundly, and especially those in which there is some disturbance of growth or body type, I have leaned toward extracts made from the whole ovary. Whether or not this distinction is well taken it is difficult to decide, especially in view of the fact that the results in all forms of ovarian therapy are unfortunately still very inconstant.

Both the ovarian and the corpus luteum extracts are prepared by various pharmaceutical firms in the form of tablets or capsules, suitable for administration by mouth (lutein, extract corpora lutea, etc.). A soluble form for administration hypodermically (intramuscularly) has also been prepared. Good results from its use have been reported by Hirst and others, but this form of medication has not as yet achieved a very wide vogue. Its results in my own hands have been encouraging.

Recently Graves has suggested the employment of "ovarian residue," prepared from the ovary after separation of the corpora lutea. While it is too early to draw conclusions as to its value, there is little reason to expect that it will prove any more effective than other ovarian preparations.

Some authors, as well as some manufacturers, lay much stress on the superiority of preparations made from the corpora lutea of pregnant as compared with non-pregnant animals. The correctness of this view is open to question, especially when we consider that the corpus luteum of pregnancy, in spite of its large size, is normally associated with an absence of menstruation. There can be little doubt that the physiologic rôle of the corpus luteum hormone varies at different stages, as asserted by Seitz and his coworkers. This investigator isolated from the corpus luteum of beef ovaries, at different stages of its development, two substances of almost opposite physiological action. One of these, which he calls lipamin, is said to stimulate the growth of both the internal and external genitalia in animals, while its subcutaneous injection in amenorrheic women will bring on the menses. This substance predominates in the young corpus luteum. The second substance, on the other hand, which Seitz calls luteolipoid, appears to act as an inhibitor of the menstrual function, and is found in large amounts in the later stages of the corpus luteum.

Types of Menstrual Disorder in Which Organotherapy is Indicated

Amenorrhea.—Menstrual and Developmental Disorders of Puberty.— During the first year or two of menstrual life, periods of amenor-

rhea are commonly observed, lasting from two to several months. This may occur even in girls who are entirely healthy in every respect, i. e., who are not suffering from such conditions as anemia, tuberculosis, etc. This physiological amenorrhea requires no treatment except perhaps reassurance of the patient. If, on the other hand, menstruation does not appear at the normal age, and if such a primary amenorrhea is associated with other evidences of lack of development, it is reasonably certain that there is some disturbance of endocrine function. Unfortunately it is not always possible, in the present state of our knowledge, to determine just what the endocrine defect is. In the majority of cases, it is probable that the fault lies with the ovaries or the pituitary, and hence administration of extracts from these glands is indicated. For reasons which I have already indicated, my preference in this group of cases is for extracts made from the entire ovary rather than from the corpus luteum alone.

In certain cases delayed puberty appears to be a manifestation of hypothyroidism, although, as will be emphasized later, the latter condition more frequently causes menorrhagia than amenorrhea. Finally, in cases which fail to respond to other organic extracts, some resort to the use of thymus or pineal gland substances, although the results are rarely striking. On the whole, it is obvious that the treatment of the menstrual and developmental disorders of puberty by means of ductless gland extracts is as yet extremely unsatisfactory, owing to our lack of knowledge of the pathologic physiology of these conditions. The use of extracts in these disorders is almost entirely empirical and often disappointing.

On the other hand, organotherapy in cases of this type, is, in my judgment, infinitely safer than the administration of emmenagogues. The extracts themselves are of course not emmenagogues, except in the very indirect sense that they may correct the endocrine defect which is responsible for the amenorrhea. On the other hand, the employment of emmenagogues, so frequently resorted to in the past, is based on the theory that they give rise to a pelvic hyperemia which promotes menstruation. Even if this were true, it would be hard to conceive how such an artificial pelvic hyperemia could induce the occurrence of the normal rhythmic menstrual flow. Furthermore, the prolonged administration of such drugs, through the persistent pelvic congestion which they entail, may easily predispose to serious pelvic discomfort and disease.

Functional Amenorrhea of Later Life.— Much of what has been said with regard to the functional amenorrhea of puberty applies also to the functional amenorrhea of later life. I need scarcely say that we are not here concerned with those cases which are clearly secondary to such debilitating systemic conditions as tuberculosis or anemia. The most common type of functional amenorrhea is that which is associated with *adiposogenital dystrophy* (dystrophia adiposogenitalis) or Fröhlich's syndrome (Chapter XXIV). I shall not go into the discussion here of this interesting condition except to say that its two principal characteristics are obesity

and sexual hypoplasia. The latter manifests itself most conspicuously in the woman by scantiness or absence of the menstrual flow. Practically all the older text books of gynecology mentioned adiposity as a cause of amenorrhea. Instead of adiposity causing amenorrhea, or vice versa, as some have believed, we know now that both conditions are themselves the result of the same underlying cause, i. e., deficiency of the pituitary body, as has been so clearly demonstrated by Cushing and his coworkers.

The rational treatment of amenorrhea of this type would seem to be the administration of pituitary substance to counteract the hypopituitarism which has been shown to be responsible for the condition. Although the amenorrhea in patients of this type is perhaps in an immediate sense of ovarian origin, it would seem that the primary defect is in the pituitary hormone, and that treatment should be directed to the correction of this latter deficiency. The results yielded by such medication have not, however, been altogether satisfactory, partly, perhaps, owing to the uncertainty which still exists as to the relative importance of the anterior and posterior lobes of the pituitary in bringing about the syndrome (Chapter XVIII).

In accordance with the formerly predominant opinion on this point, the extract which was at first most generally used was that from the posterior lobe. Fromme, who was a pioneer in this form of treatment, reported encouraging results in a series of 12 cases of amenorrhea treated in this way. In 5 of these the treatment failed, and in 2 its success was doubtful. In the remaining 5, however, the return of menstruation was prompt. Even in those in which the amenorrhea persisted, the subjective symptoms are said to have been greatly ameliorated. Hofstätter has also reported very favorable results from the use of pituitary substance in a large series of cases of amenorrhea.

Similar results are reported in small series of cases by Fries, Zöppritz, and Kosminski. The plan of treatment recommended by the last named author consists in injecting 1 c.cm. of the soluble extract (pituitrin, pituglandol, etc.) on alternate days. In one case of amenorrhea thus treated, a series of ten injections was followed by a profuse uterine bleeding. He has never given more than twenty consecutive injections to any patient. He advises frequent careful examination of the urine, on account of the danger of glycosuria.

As already intimated, the extract of the anterior pituitary lobe, rather than the posterior lobe, is now considered by most authors to be indicated in the treatment of these cases. Thus, Roblee has recently reported a successful result from the use of the anterior lobe extract in a case of adiposogenital dystrophy occurring in a male. Similar observations have been made by others.

In my own experience, the best results in the treatment of adiposogenital dystrophy have been noted from the use of thyroid extract and the various forms of ovarian extract. As regards the latter, I may say that my preference has been for extracts made from the corpus luteum alone, although

I am frank to say that the results have not been very different from those observed from the use of extracts of the entire ovary. As a matter of fact, it is rare to note reëstablishment of the menses from either form of medication. Furthermore, contrary to what one might theoretically expect, there appears to be very little influence exerted by either ovarian or corpus luteum substance on the obesity characteristically associated with the amenorrhea of these cases. Often, as a matter of fact, there is a tendency to increase rather than to decrease the body weight.

The organ extract which, on the whole, I have found most valuable in the treatment of adiposogenital dystrophy, as well as of other forms of functional amenorrhea, is thyroid extract. This is true even of those cases where there are no clinical indications of hypothyroidism. It is difficult to explain the good results not infrequently obtained from thyroid extract in these cases, nor will they be susceptible of explanation until our knowledge of endocrine relationships is far more advanced than it now is. The administration of thyroid in proper dosage is often followed by reappearance of the menses, and practically always by a more or less marked reduction in body weight.

The average dosage of thyroid extract in these cases of mild hypothyroidism should never exceed five grains a day, and in most cases it will be much less. The patient should be observed at least once a week, to determine her tolerance and to make sure that no harm is resulting from the use of the thyroid. The principal criterion should be the condition of the heart. If the heart rate is not accelerated, one may feel assured that no hyperthyroidism exists. If, on the other hand, it is found that the use of the thyroid is accompanied by a gradually mounting pulse rate, together with nervousness, tremor, etc., the dose should be cut down. For prolonged administration one or two grains a day is often sufficient.

An important guide to the action of thyroid extract is its effect upon the body weight, which is practically always diminished. This, as is well known, is the result of a stimulating effect upon the oxidation processes in the body. It is seldom advisable for the patient to lose weight at a faster rate than two or three pounds a week. The total loss of weight depends, of course, upon the initial body weight and upon the duration and intensity of the treatment, as well as upon such adjuvant measures as dietetic regulation, exercise, etc. In suitable cases the treatment yields striking results within a month, menstruation becoming normal and the health being improved in every way. Instead of discontinuing the thyroid medication abruptly, it is wise to diminish the dosage gradually, and to keep up small doses for a considerable period of time.

The probability that most of these cases are to be looked upon as really of pluriglandular origin, and the uncertainty of action of the various individual extracts has led many to resort to polytherapeutic measures in the management of these cases. Thus, in adiposogenital dystrophy, I have often used thyroid and corpus luteum extracts together with good results.

There would seem to be much justification for this, especially since the addition to the thyroid of corpus luteum in any ordinary amount is unattended with danger. Certain proprietaries are stated to contain extracts of a number of the ductless glands in varying proportions and amounts. The "gunshot" nature of some of these polyglandular mixtures indicates how important a rôle empiricism, based on a few small molecules of fact, plays in our modern efforts at organotherapy.

Uterine Hemorrhage.— In a certain proportion of cases, menorrhagia or metrorrhagia at the time of puberty is due to definite pathological lesions in the pelvic organs, such as disease of the endometrium, neoplasms of the ovary, etc. With this type of bleeding we are not here concerned. Very frequently, however, hemorrhage at this period of life occurs in the entire absence of any demonstrable pelvic disease (Chapter XXII). As a rule, it is the result of one form or another of endocrine disturbance, most frequently in the thyroid gland or the gonads. I know of no reliable observations incriminating any of the other ductless glands, although it is of course quite possible that they may at times play a rôle in the causation of uterine hemorrhage.

With regard to the *thyroid,* there has been some difference of opinion as to the effects of hyper- and hypothyroidism upon the menstrual function. The weight of evidence supports the view that, generally speaking, hyperfunction of the thyroid, as in Graves' disease, tends toward diminishing the amount of the menstrual flow, while on the other hand, hypothyroidism is more likely to be associated with excessive menstruation. This is the view which is supported by Hertoghe, as well as by Sehrt. The latter found, in a series of 55 cases of uterine bleeding of "idiopathic" origin, fully 38 which exhibited definite signs of hypothyroidism. On the other hand, there can be no question that at times menorrhagia is observed in women with undoubted hyperthyroidism, as in some cases of well marked Graves' disease. These apparent paradoxes are, of course, not uncommon in the field of endocrine pathology. As yet no satisfactory explanation can be offered for them, although it is probable that many, perhaps most, of the recognized clinical syndromes are the result of pluriglandular rather than uniglandular involvement. Hence the not infrequent overlapping of symptoms.

The menorrhagia of *hypothyroidism* is at times observed in girls in whom menstruation has appeared late and in whom there are other evidences of tardy development. The diagnosis of its hypothyroid origin is usually suggested by the existence of a more or less complete array of the symptoms which are now generally recognized as indicative of defective function of the thyroid. These I shall not detail here, except merely to emphasize the importance in this connection of obesity; the transitory "white indolent edema" which may be noted in the eyelids, cheeks, feet or fingers, and which does not pit on pressure; the harsh, dry skin, with tendency to chilliness; and the hirsute derangements, such as falling out of the hair or thin-

ness of the eyebrows, especially in their outer third. (For further discussion see Chapters XXII and XXIV.)

The treatment of uterine bleeding of hypothyroid origin is simple enough, consisting essentially in the administration of thyroid extract. It must not be forgotten that this substance is a powerful agent, whose use must always be rigidly supervised by the physician. Excessive dosage gives rise to the characteristic symptoms of hyperthyroidism, such as tachycardia and tremor. When abuse of the drug is protracted, serious injury may be inflicted upon the cardiovascular system. Seldom should the dosage exceed five grains a day. As a rule it will be considerably less, especially when the administration of the extract is to be kept up for a long time.

Pituitary extract has also been employed in the treatment of uterine hemorrhage. When the latter is due to atony of the uterine muscle, as in postpartum or postabortive cases, the results are, as is well known, highly gratifying. This can not be said of uterine hemorrhages of other types. The feeding of pituitary extracts by mouth is attended with as little success in the usual case of non-obstetrical uterine hemorrhage as in most other conditions in which it has been used. Somewhat more satisfactory appear to have been the results when pituitary extract has been given subcutaneously or intravenously. The latter method, in the hands of Kalledey, is stated to have yielded good results. Such reports, however, are still too few to make any great impression on therapeutic practice. In spite of Kalledey's contention to the contrary, it seems likely that the hemostatic effect exhibited by posterior lobe extract in these cases is due to the resulting tonic contraction of the uterine muscle, rather than to any corrective endocrinal effect.

Organotherapy of Functional Hemorrhages of Puberty and Menopause. Special consideration should be given the type of functional hemorrhage which is seen so characteristically at the two extremes of menstrual life, and especially at the menopausal age. The general management of these cases has already been outlined in Chapter XXII. From the standpoint of organotherapy, the principal difficulty is presented by the fact that we as yet know little of the endocrinopathy responsible for this form of menstrual disorder. As a matter of fact, it seems quite probable that the nature of the internal secretory disturbance varies in different cases. It is not surprising, therefore, that the results of this plan of treatment, semi-empiric as it must be, have been far from satisfactory. The organ extracts which deserve consideration in this connection are those of the thyroid, ovary and pituitary.

In the case of the functional hemorrhage of puberty, thyroid extract has, in my own hands, yielded the most encouraging results. To illustrate, in a recent case of persistent and profuse bleeding in a girl of fourteen, curettage seemed indicated, especially for diagnostic purposes. Microscopic examination of the curettings showed typical hyperplasia of the endometrium. The bleeding, however, did not cease. The patient was then given doses of thyroid extract of two grains a day, with almost immediate cessation of the

bleeding. It is only fair to add, however, that similar medication in other cases has appeared to be of no benefit, indicating, as has already been emphasized, that the endocrine disorder is not always of the same character.

In the more frequent cases of functional climacteric hemorrhage, I have rarely seen any benefit from thyroid medication, and not infrequently the bleeding has seemed to be exaggerated. Somewhat better results have followed the administration of ovarian extracts, especially of the corpus luteum preparations. This is in keeping with recent histological investigatons, which indicate that corpora lutea are commonly absent in cases of hyperplasia of the endometrium associated with uterine bleeding. In other words, even though we are perhaps dealing in these cases with a form of ovarian hypersecretion, it is not the corpus luteum which is overactive. Some other element in the ovary is concerned with the hyperfunction, the corpus luteum being deficient.

My most encouraging results have been obtained from the exhibition of corpus luteum extracts, either alone or in combination with small doses of thyroid. The corpus luteum is usually given in doses representing five or ten grains of the dried extract three times a day. Or it may be administered subcutaneously in the form of the soluble extract, which is now prepared commercially in convenient ampoule form (1 c.cm.). One ampoule is injected usually every second or third day, depending on the severity of the hemorrhages. By such measures the condition may in some cases be improved, so that the patient can be tided over the period of endocrine instability which predisposes to the development of this symptom. As to the use of pituitary extracts, little of a definite nature can be stated. The use of posterior lobe extracts has been lauded by some. As I have stated above, however, any good results obtainable from these are probably due to the well known effects of these preparations in stimulating contraction of the uterine musculature. The other effects of these substances are of such potency, however, as to contraindicate their continued administration for a prolonged period. Anterior lobe extracts have achieved no important place in the treatment of these troublesome cases, and, indeed, there would seem to be no especial rationale for their employment.

It is unfortunate that we cannot be more explicit in suggestions as to the organotherapy of this exceedingly important type of hemorrhage, and that our efforts to attack it along what seem to be rational lines have not met with a greater measure of success, but I believe that what has been said above represents the worth while in our present knowledge of the subject.

Vasomotor Symptoms of Menopause.— The principal field of usefulness of ovarian or corpus luteum preparations is in the treatment of the troublesome subjective symptoms so often observed at the menopause, and especially those due to vasomotor disturbance of one form or another. Under this head are to be placed the hot flushes and the "flashes" of heat, which constitute the most characteristic and at the same time the most troublesome symptoms of the climacterium, whether natural or artificial. Drugs are of

little service in the relief of this group of symptoms. It is here that the organ extracts have one of their most important gynecological applications. Burnam states that corpus luteum extracts yield great improvement in menopausal symptoms in 90 per cent of cases, and I do not believe that this is an overstatement. As has been indicated in a preceding paragraph, my own preference in the treatment of this group of cases is for corpus luteum preparations rather than those made from the entire ovarian substance. It is only fair to say, however, that many gynecologists report results from extract of whole ovary which are, to say the least, equally as good as those observed from the administration of corpus luteum preparations.

In view of the rather large number of commercial preparations of both ovarian and corpus luteum extracts, it is scarcely possible, in this discussion, to suggest definite dosages. Speaking generally, it may be said that the average dose of corpus luteum extract advisable in the treatment of menopausal symptoms is about five grains, three times a day, of the dried substance. There are some who recommend much larger doses than this (Hill, Burnam), but I have personally seldom seen good results from very large doses when smaller ones had failed to improve the patient's condition. A great comfort in this form of treatment is the fact that the extract is, within ordinary limits, nontoxic, and hence can work no harm to the patient. Occasionally, however, prolonged corpus luteum medication with even very moderate doses may cause more or less gastric irritation.

Dysmenorrhea.— Since this chapter aims only to sketch the more important indications for organotherapy in menstrual disorders, we need make only a passing reference to the fact that some have used ovarian substances in the treatment of primary dysmenorrhea. This practice is obviously based on the doubtful theory that the underlying cause of this symptom is a hypogenitalism. At any rate, the results, so far as I have been able to learn, have been of no particular value. If ovarian extract is to be employed in cases of apparent underdevelopment of the generative apparatus, the extract made from the entire ovary would seem preferable to that made from the corpus luteum alone, for reasons which have already been indicated.

There are good grounds for believing that primary dysmenorrhea is due to a hypopituitarism rather than to a hypogonadism (see Chapter XX). Certainly this statement would seem to be correct, as applied to the uterine hypoplasia which is seen so characteristically in patients suffering from this form of menstrual pain. The administration of pituitary extracts in these cases would appear to be a rational procedure, the preference being for anterior lobe extracts, or perhaps better, for the whole gland substance. This, according to Götsch, should be given in initial doses representing five grains of the dried gland three times a day, increasing the dose gradually, if necessary.

XXVI

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CHAPTER XXVII

THE TREATMENT OF MENSTRUAL DISORDERS BY RADIUM AND X-RAY

By Howard A. Kelly, M. D., and Curtis F. Burnam, M. D.

Introduction.— The microscopic changes in tissues subjected to radium or X-ray radiation are very similar and the general physiological effects induced in an individual woman through X-ray or radium sterilization are so nearly the same, that it seems logical as well as corvenient to consider these two therapeutic agents together.

It should not be assumed, however, that they are necessarily exactly equivalent and that they can, in every instance, be used interchangeably; for it is certain that many cases are much more easily and effectively treated with intra-uterine radium than by any transabdominal method. This difference is striking when a rapid and complete amenorrhea is sought. When a considerable amount of radium is available for transabdominal radiation, the operator can secure more easily the desired changes in the ovaries and uterus than by X-ray methods, and certainly with less risk to the skin and underlying integument. It is only fair to state, however, that the authors have been much more concerned with the development and employment of radium than X-ray technics.

History.— William James Morton, the first to demonstrate that uterine hemorrhage due to myomata could be helped by X-raying the tumor through the lower abdomen, reported his cases in the New York Medical Record of the issue of July 25, 1903. It was more than three years later when radium in the uterus was first used for the same purpose by Oudin and Verchere, two French observers who reported their experiences in the Ann. d'Electrol., Oct. 31, 1906. Oudin also published a report in the same journal in August, 1907.

In addition to the customary inertia which must be overcome to introduce any new method of doing things, three definite factors militated against the wide acceptance and employment of these agents. There was, first of all, a successful, well developed and widely applied surgical treatment which had been won only after the great labor and toil of more than a decade; secondly, the ray treatment was uncertain and on account of its duration — often months — was very trying to the patience of both the physician and the patient; thirdly, and finally, in not a few cases painful and dangerous skin burns followed the treatment.

It is not surprising, therefore, that, in spite of the good results obtained

by the occasional and desultory use of X-ray by röntgenologists, the method had no wide acceptance and did not take its place in the gynecological armamentarium until after Professors Krönig and Gauss of Freiburg had developed a technic which was curative in a few months from the beginning of treatment, which did not burn or injure the patient, and which proved so uniformly successful through a long series of cases treated at the Freiburg University gynecological clinic. The publication of their studies and the conclusion drawn that a safer and more efficient way of treating uterine fibroids was by X-ray rather than by surgical procedures, met with almost universal condemnation by the German gynecologists. Nevertheless, in less than two years from 1912, the date of the principal publications from Freiburg, every gynecological clinic in Germany was busily engaged in running its X-ray machine from morning till night, and it was generally acknowledged that the new procedure was very valuable.

In this country as well as in Great Britain there has been nothing like such an acceptance or trial of either X-ray or radium by gynecologists. In France, where some of the very earliest and best work in this field was done, X-ray and radium are widely employed.

Radium has nowhere been so extensively used as the X-ray, due in part perhaps to its cost and the difficulty in procuring it. It is, however, now being employed at many of the gynecological clinics in America, and is very favorably regarded by those who have had experience with it. John G. Clark of Philadelphia, C. Jeff Miller of New Orleans, Henry Schmitz of Chicago, and many others have published most satisfactory experiences. It was, perhaps, chiefly due to the work of Cheron, which began in 1909, his first publication being in 1911 (Cheron, Arch. d'Electr. Méd., Bordeaux, 1911, xix, 355), and to our own work which began in 1911 and which was first made public at the 1914 meeting of the American Medical Association, and published in the same year (Kelly and Burnam, Jour. Am. Med. Ass., 1914, lxiii, 622), that there originated an impulse which has led to the enthusiastic and valuable work of so many physicians in this field.

Literature.— The most convenient source of literature, to those readers especially interested in the original publications, is to be found in the volumes of *Strahlentherapie*.

Most of these studies deal with the effects of ray therapy on uterine hemorrhage and fibroids. There is but scant mention of the pain feature of dysmenorrhea and, while in a number of reports there may be a paragraph or so dealing with the character, severity and frequency of menopausal symptoms sequent to the ray menopause, these are nowhere taken up as the prime object of study. So far as we are aware, there is no existing publication dealing with the ray treatment of nervous disorders associated with or in any way dependant on the periodic menstrual disturbance.

The available literature dealing with the treatment of dysmenorrhea not associated with menorrhagia is limited to the X-ray. Döderlein (Döderlein, Monatschr. f. Geburtshülfe u. Gynäk., xxxiii, Hft. iv, 413) states that

the dysmenorrhea of young patients is favorably influenced by X-ray treatment. Eymer and Menge (Eymer u. Menge, Monatschr. f. Geburtshülfe u. Gynäk., xxxv, Hft. 3, 268) saw benefit for one period in two cases. Fränkel (Fränkel, Berl. Klin. Wchnschr., Nr. 34, 1610) holds that ovarian dysmenorrhea, but not uterine, can be benefited. Reifferscheid (Reifferscheid, Strahlentherapie, vol. iv, 1914, p. 146) in a series of five cases had one marked improvement, two temporary improvements, and one slight improvement. Such is the scant literature we have found dealing with this important subject.

Anatomical Changes Observed in the Ovaries and in the Uterus After Radiation.— Practically all the histo-anatomical investigations that have been published are limited to a study of the effect of radiation on the ovaries, and this doubtless explains why it was held for so long that the ray effect on uterine fibroids and hemorrhage was entirely an indirect one through the ovaries. We know now that this is only partially true.

As early as 1903, it was already recognized that marked degenerative changes were induced by intense radiation of either the male or female generative organs, and that consequent sterility followed. Splendid studies are those of Reifferscheid (Reifferscheid, Strahlentherapie, 1915, vol. v, p. 407) and Cl. Regaud and Lacassagne (Cl. Regaud et Lacassagne, Jour. de Physiotherap., Oct. 1913, 546, 550). The most vulnerable part of the ovary is the graafian follicle, the ovum and granulosa layer being the first to show disintegration. The germinal epithelium and the corpus luteum are much more resistant. In some experiments with animals marked changes have been shown within twenty-four hours, but the summit of change after a single treatment may not be reached for six weeks. The primordial follicles stand intermediary in vulnerability between the graafian follicles and the corpus luteum tissue. Under very heavy radiation they too may be completely destroyed. As a rule, however, only a part of them are destroyed and the others are subjected in their ripening to a period of inhibition, varying from one to several months in animals, while in human beings, according to our clinical experiences, it is common for this period to extend over from one to three years.

The anatomical changes in the uterus dependent on radiation are much more difficult to interpret and much less characteristic than those observed in the ovaries. When permanent amenorrhea is induced, the entire uterus, corpus and cervix, shrink markedly in volume. This decrease in size is associated with relatively marked diminution in the musculature, with endarteritic changes in the blood vessels, and with a decided thinning of the glandular part of the endometrium. Where there has been an intractable tendency to the formation of a polypoid endometrium, a single intrauterine treatment of mild intensity may cause it to disappear permanently. This is well established in several cases under personal observation.

In certain uterine fibroids removed by operation after radiation, there has been observed the destruction of cell nuclei and the running of the

chromatin into large lakes, a change characteristic of ray destruction of many malignant tissues. From these changes, in general corresponding to those familiar in the senile uterus, observed in some cases, there is a gradual lessening until no alteration whatever can be definitely described.

The Ray Menopause.— In our very first observations, the almost complete absence of hot flushings, sweatings, and the nervous manifestations which we had grown to expect with öophorectomy amenorrhea, astonished us. A consideration of the anatomical changes already described makes this easily understandable — the existing corpora lutea persist for several months, the primordial follicles, or some of them, indefinitely. Nevertheless, a considerable number of radium amenorrheas are associated with distinctive menopausal disturbances.

In a continuous series of 110 cases, 50 per cent made no complaint, about 25 per cent made slight complaint and almost 25 per cent complained of pronounced flushings. Not one patient considered the hot flushings or nervous disturbances disagreeable enough to make her regret the treatment. The usual expression has been that the general improvement in health and well being has been pronounced.

It should be of some weight in this connection to state that the general psychic atmosphere in many of these patients has not been of the best. Well meaning friends have suggested premature aging, loss of mind, etc., as a consequence of the treatment.

We have had some experience with patients predisposed or actually psychically disturbed and have noticed no tendency in the treatment to precipitate attacks of mental upset. However, it is possible that this might follow in some cases, and the matter cannot be definitely adjudged except after prolonged investigation.

The Technic of Radiation.— The reader is referred to the original literature appended for his convenience at the end of this chapter, and is advised to see personally the actual carrying out of X-ray and radium treatments in the hands of those familiar with them, before personally undertaking either.

The X-ray technic of Gauss and Lembcke consists in the individual maximum dosage of the pelvic organs at intervals of from four to eight weeks until the desired result is obtained. With the X-ray tube at a focal distance of 15 cm. and the rays filtered through at least 3 mm. of aluminum, the treatment is given through a number of portals on the skin of the lower abdomen and back. The use of many portals secures adequate inside dosage without endangering the skin at any one point. The replacement of the old water cooled air tubes by the now universally used Coolidge tube has made the treatment more economical and has greatly simplified the accurate measurement of the dosage given.

When radium is used from the abdomen, two or three portals are advisable at a distance of from 5 to 15 cm. from the skin. The filtration should be through 3 mm. of lead. Comparatively large quantities of radium are

desirable, if not absolutely necessary. The average dose where a complete amenorrhea is desired is 24,000 mg. hours. Treatment should not be repeated within four weeks.

In intra-uterine radiation, the radium in a convenient applicator is so placed or moved that the entire surface of the uterus gets an equal treatment, amounting on the average to about 1,500 mg. hours.

There is a wide variation in the dosage necessary to bring about amenorrhea. If it is desirable to do so, however, it is always possible to produce it at a single treatment by a combination of inside and outside radiation. Overradiation inside may produce discharges and pain for weeks, but it is never necessary to cause these symptoms. But little difference has been noted in young subjects and those over forty in their response to inside radiation, although there is quite marked difference when the treatments are given transabdominally; and by X-ray it is sometimes impossible to attain a complete result in young patients.

Classification of Dysmenorrhea from the Ray Therapy Standpoint.— While no sharp separation of the various disturbances of menstruation occurs in practice, the same patient frequently having hemorrhage and pain as well as nervous and general upset, nevertheless, for convenience in exposition, it is clearer to consider the effects on each of these phases of dysmenorrhea separately and individually. As a matter of fact, one or the other is apt to dominate the clinical picture and is essentially the real reason for the institution of treatment.

Cases with Abnormality of the Menstrual Flow.— Patients with abnormality of the menstrual flow should be divided into those who are suffering from anemia through pronounced loss of blood and those who are merely inconvenienced by prolonged or continuous bleeding. It need be recalled here that the hematopoietic system varies immensely and that one individual is not discommoded by an amount of blood loss that is dangerous to another person.

After having determined on ray therapy, the operator may choose any one of three ends. The treatment may aim at simple reduction of the intensity or duration of the flow, or it may aim to bring about an amenorrhea for a time, with the hope that during this period the patient will recover her health and that when the periods return they will be so modified as to cause no trouble, or the aim from the very beginning may be to produce permanent amenorrhea and sterility. These different aims can be met by employing different intensities of radiation. In the first group comparatively mild treatments, in the third group very heavy treatments must be employed.

Whether a complete amenorrhea is desirable in any individual case depends a great deal on the age of the patient and on her social surroundings and conditions. Unless there is a very good reason for making it permanent, it is a good working plan to produce by the first treatment a temporary amenorrhea, and to wait and see if this does not fulfil all the desirable objects of the treatment. If, on the return of bleeding, it is still

excessive, then another treatment can be carried out and the result made permanent. Before radiating a girl or young woman for excessive flow, it is imperative to try out thoroughly the simpler plans of treatment — medicinal, hygienic and curettage.

All but the most obstinate cases may thus be excluded from a treatment which might readily cause sterility. That this may be more of a theoretical than an actual danger is evidenced by two of our patients, who, after prolonged amenorrhea, had a return of menstruation, married, and each had a perfectly normal child. In older women it is less important to consider this phase of the problem and in those near the menopause a permanent amenorrhea should be aimed at. In most cases where amenorrhea of several months has been obtained, the return of menstruation has been marked by a normal flow. In a series of 164 cases of bleeding fibroids or simple bleeding uterus there has been no death and no serious consequence of any kind following the treatment, and the results in relief of the bleeding have been most satisfactory.

Finally, in patients who are not anemic and who are willing to wait for results, very mild treatments to control but not stop menstruation will, in a considerable proportion of cases treated, give satisfactory results in both reducing the flow and in lessening discomfort. A very mild intra-uterine application may be effectual in curing a tendency to bleed almost continuously but never excessively. We have seen one such patient who had lost all count of her periods and who had resisted curettages and various applications and who has, after a single treatment, been perfectly regular for several years.

Cases Characterized by Painful Menstruation.— That ray therapy should be considered in these conditions is made obvious by recalling that menstruation can be permanently done away with through its adequate use. It is equally obvious, however, that it should be used only in the very exceptional case in young women, who constitute the large majority of such patients. In older women the development of painful menstruation usually is associated with the appearance of a fibroid tumor or some tubo-ovarian complication, especially chronic pelvic inflammatory disease. The value of the treatment in uterine fibroids has been shown in many cases. Our experience with the chronic pelvic inflammatory group, as yet quite limited, is, however, most encouraging, and it is our opinion, on the basis of only six cases, all quite satisfactorily treated, that ray therapy will ultimately find here a very satisfactory and large field of usefulness. Many of the chronic pelvic inflammatory sufferers are principally upset only during the period of menstrual congestion. These patients should preferably be treated by the transabdominal route.

Radiation which aims to reduce but not stop menstruation would seem to be the method of ray treatment best applicable to the painful dysmenorrhea unassociated with organic disease of the uterus, tubes or ovaries, and which is commonest in young and unmarried women. Unfortunately the

relief obtained is usually temporary and partial. In a series of nine cases we have had one complete success of 18 months standing, two partial successes and six failures.

Cases with Marked Nervous or Psychical Disturbances Present Principally or Solely During the Menstrual Periods.— There are but few medical men who have not had experience with patients who are enormously upset during the menstrual period. Some of them are sick half or more of the time. We need not repeat here the protean symptomatology of headaches, nausea, anorexia, mental depression, etc. These patients are most frequently encountered during the early and late years of menstrual life. The clinical picture suggests autointoxication. While, as already stated on page 330, the induced ray menopause has not made patients more uncomfortable from the nervous and general functional standpoints, it has not been emphasized enough that very many of them report great improvement in these directions. This conforms with the nervous improvement frequently observed at the time of the normal menopause.

It must be constantly kept in mind, however, that many functional and nervous disturbances due to a great variety of organic conditions totally unconnected with the pelvic organs may be greatly exaggerated at the menstrual period, and as a consequence may closely simulate the menstrual intoxications. A most careful general, physical and psychic examination should be made of these patients before giving ray therapy to induce a menopause.

We have successfully treated nine such cases, three of whom felt perfectly well except at the period time. Two of the three had headaches, nausea, extreme general nervousness and weakness, and the third fearful mental depression. All have been perfectly well after the establishment of a complete amenorrhea. In two other cases almost equally satisfactory results have been obtained, although the nervousness in these was present during the entire month, and was merely greatly exaggerated at the menstrual periods.

In four cases the results were unsatisfactory. One of these was a sufferer from hyperthyroidism; another had marked religious delusions present all the time, but exaggerated during the period; a third was a typical hypochondriac neurasthenic; and the fourth a patient insufficiently treated and still menstruating.

Another interesting group has been that of four patients treated for epilepsy. In one of these, a woman of 44 years, there have been no attacks in four and a half years since her treatments. In the other three there was a distinct and marked improvement. All tended to have the attacks principally at the time of the periods.

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